OPTIMIZING OUTCOMES OF VAGINAL PROLAPSE SURGERY WITH AND WITHOUT MESH

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Voor mijn ouders

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GENERAL INTRODUCTION AND OUTLINE OF THESIS

INTRODUCTION

Prolapse is derived from the Latin word *prolabi*, which literally means 'sliding forward'. Pelvic Organ Prolapse (abbreviated as POP) is defined as the downward descent of female pelvic organs, including the bladder, uterus or post-hysterectomy vaginal cuff, and the small or large bowel, resulting in protrusion of the vagina, uterus or both.[1] The anterior vaginal wall is the most typical compartment of the vagina to prolapse.[2] This type of prolapse usually includes descent of the bladder: when the bladder protrudes, this is called cystocele. Apical prolapse entails either the uterus or post-hysterectomy vaginal cuff and can affect the small intestine (enterocele), bladder, or colon (sigmoidocele). Posterior vaginal wall prolapse concerns the rectum (rectocele) but can also include the small or large bowel.[1]

Women who develop Pelvic Organ Prolapse can present with one symptom, such as vaginal bulging or pelvic pressure, or with several, including many bladder, bowel and pelvic symptoms. The hymen seems to be an important cutoff point for symptom development.[3] Of all symptoms presented, the only one that is acknowledged consistently by patients with severe prolapse is the presence of a vaginal bulge that can be seen or felt.[4, 5]

Uterovaginal support can be measured with the Pelvic Organ Prolapse Quantification (POP-Q) system and can broadly be classified in 4 stages, ranging from 0 (perfect pelvic support) to IV (total procidentia or complete vaginal eversion).[6]

HISTORY

Vaginal prolapse typically is a condition that affects women and is of all times. Soranus, a Greek physician and medical writer reported on vaginal prolapse already in the 2nd century AD. He believed that a vaginal prolapse could be caused by falling to the ground, which consequently caused the rupture of the suspending structures of the vagina. On the other hand, circumstances that cause severe emotional stress, such as the loss of a child or even a heavy storm at sea (!) were also considered to be causes of prolapse of the uterus or vagina.

Some centuries before Soranus, Hippocrates had advised women with prolapse to be hanged upside down on a vertical standing ladder for 24 hours to enable gravitational forces to reduce the vaginal prolapse of these women (figure 1). After the 'natural' repositioning of the prolapsed vagina, it was stuffed with a lemon or pomegranate to keep the uterus and/or vagina in place.

Digital repositions and stuffing of the vagina with a sponge soaked in diluted vinegar or sour wine are reported as well in ancient times.

Reinier de Graaf *(Reijnerus de Graeff, 1641-1673)* (figure 2), physician and anatomist in Delft, has devoted a chapter in his book 'De mulierum organis generationi inservientibus tractatus novus' (1672) to the diagnosis and therapy of the prolapsed uterus:

> *Soo nu de Lijf-moeder tegelijk uyt haar oude plaats nederwaarts sakt, benamen wy dit neder-dalen 't uytsakken des Lijf-moeders; 't welk na dat het veel of weynig is,*

soo glijt somtyts de Lijf-moeder halverweegs de Scheede, somtyts tot aan den in gang des selfs toe, en snapt by wylen ook wel gants by de Schamelheydt uyt, op allerhande manieren beleedigt; jaa soo, dat eenige genootsaakt sijn geweest deselve af te setten; waar van gedenk-waardige Voor-beelden sijn te sien.

De Graaf reported of some examples that demonstrate that

Vrouwen sonder Lijf-moeder (alhoewel het weg-neemen om de veel-voudige Vaten, die deselve bekruypen, seer gevaarlijk is) nogtans kunnen leeven.

After having performed a postmortem examination on a woman in the 'Gasthuis' in Delft, De Graaf reported in 1671 on the use of certain pessaries for vaginal prolapse. These were made of cork and covered with wax to keep the uterus or vagina in place:

Welke met een uyt-gesakte Lijf-moeder hadt gegaen: wy vonden dan in de Scheede geen vleesig oft' eenig ander uyt-wasch, maar alleen een groote wassen-bol, door welkers in-sitten de Scheede (die andersins, om 't seer verslappen der Banden des Lijf-moeders wierde om-gekeert en buyten uyt-hing) nu met de Lijf-moeder binnewaarts wierd' op-gehouden. (Source: History of treatment of POP, unpublished work by A.L.Milani, H.L.Houtzager and M.E.Vierhout)

Figure 1. Repositioning of utero-vaginal prolapse of a woman at the time of Hippocrates

Figure 2. Reinier de Graaf, physician and anatomist in Delft (1641-1773)

PREVALENCE

Pelvic Organ Prolapse is a highly prevalent condition that may affect 50% of parous women, causing a variety of urinary, bowel and sexual symptoms that may be associated; however, not all of these women are bothered by this condition.[7] Despite the fact that pelvic organ prolapse is one of the most usual indications for gynecologic surgery, epidemiological studies on incidence and prevalence are rare and usually

based on clinical populations or surgical registries. In one multicenter study of 1006 women aged 18-83 years presenting for routine gynecological care, 24% had normal support and 38% stage I, 35% stage II and 2% stage III Pelvic Organ Prolapse.[3]

A large Dutch cross-sectional study among community dwelling women aged between 45 and 85 years, demonstrated a prevalence rate of symptomatic POP of 11.4%.[8] Of these women 36.5% were diagnosed with stage I, 33% with stage II, 5% with stage III and only 0,5% with stage IV prolapse. However, only 6.9% of women diagnosed with stage I and 15.8% of those diagnosed with stage II experienced vaginal bulge symptoms as opposed to 43,3% of women with stage III and 100% of women with stage IV prolapse.[9] Thus, some loss of utero-vaginal support is present in most adult women, and if not symptomatic, should be considered physiological.

CAUSES AND RISK FACTORS

The cause of Pelvic Organ Prolapse is likely to be multifactorial, attributable to a combination of risk factors. Vaginal childbirth, advancing age and increasing body--mass index are the most consistent risk factors, of which vaginal childbirth is the most frequently associated risk factor. Compared with nulliparous individuals, the relative risk of developing prolapse was 8.4 for a woman who had delivered two children and 10.9 for someone with four or more children.[10] Every additional delivery up to five births increased the risk of worsening prolapse by 10-20%.[2] Furthermore, women with a body-mass index of more than 26 kg/m^2 are more likely (OR 3.0,1.6-5.7) to undergo surgery for prolapse than those with a lower value.[11]

Potential other risk factors are forceps delivery, prolonged second stage of labour, macrosomia, family history of POP, race, occupations entailing heavy lifting, constipation, connective tissue disorders and previous hysterectomy.[1] Maternal history of POP and symptoms of prolapse during pregnancy are proven risk factors for the development of POP as well.[8]

PELVIC ORGAN SUPPORT AND PATHOPHYSIOLOGY

Anatomical support of pelvic viscera is mainly provided by the levator ani muscle complex and connective tissue attachments of the pelvic organs (endopelvic fascia).[1] Disruption or dysfunction of one or both of these components can lead to loss of support and, eventually, pelvic organ prolapse. The muscles of the levator ani complex are tonically contracted at rest and act to close the genital hiatus and provide a platform for the pelvic viscera. Defects in the pubovisceral and iliococcygeal areas of the levator ani muscle complex have been noted on Magnetic Resonance Imaging in 20% of primiparous women, which are not seen in nulliparous individuals, suggesting that vaginal delivery contributes to the development of pelvic organ prolapse through levator ani muscle injury.[12, 13] Levator ani defects can also be detected by translabial ultrasound imaging techniques.[14-16]

The endopelvic fascia is the connective tissue network that envelops all organs of the pelvis and connects them loosely to the supportive musculature and bones of the

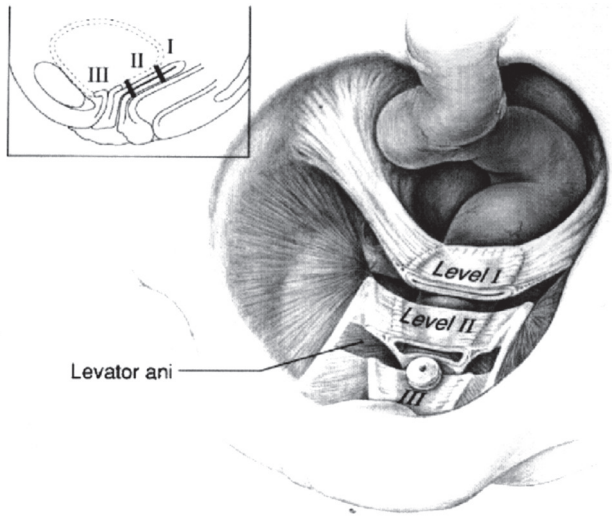

Figure 3. The 'levels of Pelvic Organ Support' (with permission of John O. DeLancey)

pelvis. DeLancey has documented three levels of fascial suspension of pelvic organs (figure 3). The upper third of the vagina (level I) is suspended from the pelvic walls by vertical fibers of the paracolpium, which is a continuation of the cardinal ligament. In the middle third of the vagina the paracolpium attaches the vagina laterally to the arcus tendineus and fascia of the levator ani muscles (level II). The vagina's lower third fuses with the perineal membrane, levator ani muscles, and perineal body (level III).[17] It's increasingly realized today that restoration of level I support is of utmost importance in securing a successful outcome in prolapse surgery.[18]

Historically, cystoceles have been divided into so-called 'displacement' and 'distension' cystoceles. Displacement cystoceles result from detachments of the endopelvic fascia from the arcus tendineus fascia pelvis, which are also known as *paravaginal* defects and were first described by White in 1909.[19] In 1976 Richardson described, next to what he called the fascia-lateral (or *paravaginal*), transverse and midline defects. The latter defects were considered to cause a 'distension' cystocele and are also known as so-called *central* defects.[20] The overall prevalence of a paravaginal defect in patients with anterior vaginal wall prolapse though is low and clinical detection poor.[21]

CLINICAL PRESENTATION

Women who develop pelvic organ prolapse can present either with only one symptom, such as vaginal bulging or pelvic pressure, or with several complaints, including many bladder, bowel, and pelvic symptoms.[1] With the exception of vaginal bulge symptoms however, none is specific to prolapse. Considerable overlap exists with other pelvic-floor disorders, and clinicians should be aware of other potential

sources for a patient's complaints. It is stressed here once more: the only symptom that is acknowledged consistently by patients with severe pelvic organ prolapse is the presence of a vaginal bulge that can be seen and/or felt.[4, 5, 22]

Lower urinary-tract complaints are frequent in women with pelvic organ prolapse. Stress urinary incontinence, particularly when prolapse is not severe, is often present.[23] Overactive bladder symptoms are clearly related to higher degrees of pelvic organ prolapse, and reports of urinary retention are frequent as well.[4, 24, 25]

Women with pelvic organ prolapse frequently complain of symptoms related to bowel dysfunction, including a feeling of incomplete emptying, straining, the need to apply digital pressure to the vagina or perineum ('splint') to start or complete defecation, urgency and incontinence. In studies on the relation between bowel dysfunction and presence and severity of prolapse, researchers have reported either a weak correlation between posterior vaginal wall support and specific ano-rectal symptoms or no link at all.[5, 22, 26] The defecatory symptom that arises most consistently with respect to posterior vaginal wall prolapse though, is the need to splint the vagina or perineum to defecate.[1, 5, 22]

Women with pelvic organ prolapse have comparable rates of sexual activity to similarly aged individuals without this disorder.[27] A third of sexually active women with pelvic organ prolapse complain that their prolapse interferes with sexual function.[28, 29] However, in a comparison of sexual function of individuals with and without prolapse, using a validated sexual-function questionnaire, no difference was noted in frequency of intercourse, libido, vaginal dryness, dyspareunia, orgasmic function, or overall sexual function between the two groups.[27]

MANAGEMENT

Management options for women with symptomatic pelvic organ prolapse include observation, pelvic physiotherapy, the use of a pessary or surgery.

Not every woman with pelvic organ prolapse presents with symptoms or bother. This is especially true for women with prolapse that does not extend beyond the hymen. Explanation and reassurance and a 'watchful waiting' strategy in such cases is appropriate. However, signs of obstructed urination or defecation, vaginal erosions or hydronephrosis due to ureteral kinking are indications for treatment, even in women with few symptoms of their prolapse.[1]

Evidence for the efficacy of pelvic floor muscle training in the management of pelvic organ prolapse is so far minimal.[30] There is only one study suggesting that daily pelvic floor muscle strengthening can slow the progression of anterior vaginal wall prolapse in elderly women.[31]

The use of a pessary (figure 4) can be an effective treatment for symptom relief in women with pelvic organ prolapse, particularly for those who do not opt for surgical treatment. Ancient pessary treatments with halve pomegranates soaked in sour wine and corks covered with wax, have today been replaced by modern elastic silicone objects of various shapes and sizes which can be used by women of all ages. Most frequently used devices are rings, rings with support, Gelhorn and donut pessaries.

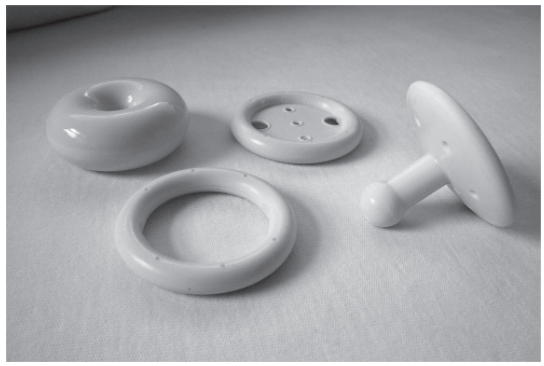

Figure 4. Examples of frequently used pessaries (from Lamers et al)

The use of a pessary is able to adequately relieve many symptoms of POP and may contribute to improvement of quality of life scores in women suffering from POP.[32]

A vast group of women however seems to prefer surgical correction of the aberrant vaginal anatomy. In 2003, more than 300.000 women underwent prolapse surgery in the United States, indicating that POP is among common indications for surgery.[33] Precise data for the Netherlands are difficult to distract, for since 2005, 20 of 97 Dutch hospitals no longer supplied data on their operative procedures to the LMR (Landelijke Medische Registratie). However, it is been calculated that the number of hospital admissions for POP per year between 2001 and 2009 in the Netherlands has increased with 50% to a roughly estimated 13.000 per year (Source: Kiwa Prismant, and personal communication R.J.Detollenaere).

The surgical treatment of POP can be broadly categorized into reconstructive and obliterate techniques. One example of the latter is the colpocleisis according Le Fort (France) or Neugebauer (Germany), that corrects pelvic organ prolapse by moving pelvic viscera back into the pelvis and closing off the vaginal canal either partially or totally.[34, 35] Reconstructive surgeries for prolapse aim to correct the prolapsed vagina while maintaining (or improving) vaginal sexual function and relieving any associated pelvic symptoms. Although either an abdominal or vaginal route can be undertaken for surgery of pelvic organ prolapse, the majority of procedures is performed vaginaly.[36, 37]

With the increasing life expectancy and the changing lifestyle of elderly women, one may anticipate on a further increase in the demand of POP surgery in the nearby future (source: CBS and Sociaal & Cultureel Planbureau). This is already expressed in recent data on the lifetime risk for a woman to undergo a single operation for POP or UI, which has been adjusted upwards from 11% in 1997 to 19-20% at present.[37-39]

WHY THIS THESIS?

Fifteen years ago an important scientific paper on the epidemiology of surgically managed pelvic organ prolapse (POP) and urinary incontinence (UI) was published.[37]

At that time the authors were probably not fully aware of the revolutionary swing they had caused in urogynecological research and consequently the development of new POP repair techniques.

Two conclusions in this paper were considered a challenge and thus became the inspirational source of this thesis.

'Pelvic floor dysfunction is a major health issue for older women, as shown by the 11,1% lifetime risk of undergoing a single operation for pelvic organ prolapse and urinary incontinence, as well as the large proportion of reoperations (29.2%), and the time intervals between repeat procedures that decreased with each successive repair.'

1st challenge; is it possible to reduce recurrence rates and increase durability of POP repairs?

'The long-term efficacy of pelvic floor surgery should be determined. Valid outcome assessment will require the development and application of a comprehensive and standardized assessment of patient symptomatology, pelvic organ support and pelvic floor function, before and after surgical intervention.'

2nd challenge; is it possible to optimize assessment of symptomatology and the anatomical and functional outcomes of prolapse repairs?

This thesis is an attempt to honour and respond to these two challenges.

First challenge. The evolution of vaginal surgical repair techniques

In the nineteen eighties, the years in which the author started his residency in Obstetrics & Gynecology, the common surgical treatment for a patient with POP, was an anterior and posterior colporrhaphy, combined with either trachelectomy or a vaginal hysterectomy.[40] This 'confection-like' approach to the POP phenomenon gradually changed in the nineteen nineties of the former century to a more 'tailored' repair of POP.[41-43]

Another development was the use of supportive mesh, biological or non--absorbable synthetic, with the principal aim to reinforce traditional native tissue repairs, whereby the mesh was used as an overlay to augment the durability of traditional colporrhaphies.[44-49]

Parallel to that development, and inspired by the success of the 'transobturator route' of the tension-free vaginal tape to treat stress urinary incontinence as well as the superior results of non-absorbable synthetic mesh to native tissue repairs in inguinal hernia surgery, a collaborative group of French gynecologists invented the Tension Free Vaginal Mesh (TVM) technique, which was a whole new approach to the surgical repair of POP.[50-52] This resulted in a technique that was 'blind' and 'trocar- guided', and that avoided traditional colporrhaphy and at the same time solved the academic dilemma of how to treat a 'central' or 'paravaginal' anterior wall defect.[53] In 2005 the first commercially available 'mesh kit' (figure 5) was launched on the market and the first results of this trocar-guided tension-free vaginal mesh insertion (Gynecare Prolift Pelvic Floor Repair System™, Ethicon, Somerville, NJ, USA) were published in 2007.[54]

In 2008 the next attempt was undertaken to improve mesh surgical outcomes and improve biocompatibility with the introduction of a new lighter-weight, partially

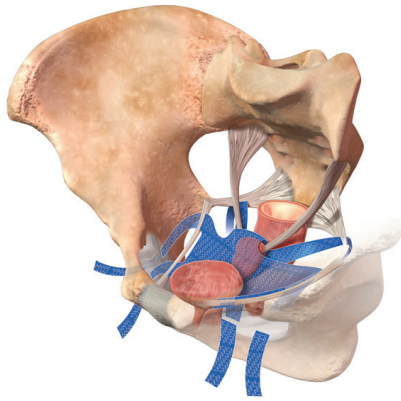

Figure 5. Total Tension-Free Vaginal Mesh schematically inserted (Prolift™ Kit) (with permission of Ethicon Women's Health & Urology, Amersfoort, the Netherlands)

absorbable mesh, which aimed to reduce some of the adverse effects of the previous heavier-weight meshes, which were particularly related to mesh contraction.[55, 56] The first one-year outcomes of an observational cohort study on the trocar-guided insertion of this new light-weight and partially absorbable mesh were published in 2011 and are part of this thesis.[57]

Second challenge. Tools to standardize and quantify treatment outcomes

I. Pelvic Organ Prolapse-Quantification (POP-Q)

One year in advance of the publication of the Olsen paper, Bump et al published a scientific paper on the consensus on the standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction.[6] This article presented a standard system of terminology, which had, at that time, been recently approved by the International Continence Society, the American Urogynecologic Society, and the Society of Gynecologic Surgeons, and was meant for the description of female pelvic organ prolapse and pelvic floor dysfunction (figure 6). An objective site-specific system for describing, quantization, and staging of pelvic support in women was included, which was named the **P**(elvic) **O**(rgan) **P**(rolapse)-**Q**uantification system. It had been developed to enhance both clinical and academic communication regarding individual patients and populations of patients. Clinicians and researchers caring for women with pelvic organ prolapse and pelvic floor dysfunction were encouraged to learn and use the system.[6] Though it took time for clinicians in everyday practice in particular, but for researchers as well, to learn and use the system, it has recently been published that between the years 2004 and 2007 the use of POP-Q had increased from 64.9% to 82.1% while other grading systems, such as the 'Baden Walker half way system', decreased. POP-Q was used more frequently in the US than in other countries. Urologists used POP-Q less and Baden-Walker more frequently than other specialists. The authors concluded that POP-Q had been adopted as the universal language of prolapse quantification in the published literature.[58]

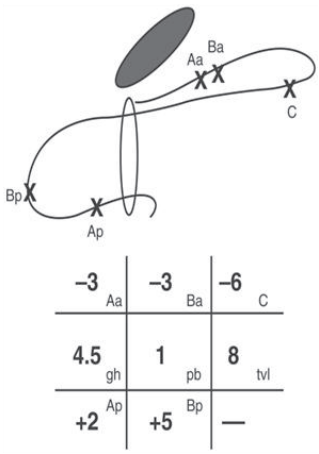

Figure 6. Example of a POP-Q registry

II. Health-related quality of life questionnaires

In 1994 Shumaker et al introduced two condition-specific instruments specifically designed to assess the Health-related quality of life of Urinary Incontinence (UI) in women: the 'Urogenital Distress Inventory' (UDI) and the Incontinence Impact Questionnaire (IIQ). Used in conjunction with one another, these two measures provided detailed information on how UI affects the lives of women.[59] One year thereafter the results of the use of the short forms of these questionnaires (UDI-6 and IIQ-7) were published.[60]

However, pelvic floor disorders not only comprehend urinary incontinence, but also prolapse and defecatory disorders. Therefore Barber et al presented the long forms and the respective short versions of the Pelvic Floor Distress Inventory (PFDI/PFDI-20) and the Pelvic Floor Impact Questionnaire (PFIQ/PFIQ-7), two condition--specific quality of life instruments for women with pelvic floor disorders, that were based on the UDI, but had additional questions regarding pelvic organ prolapse and colorectal dysfunction, in 2001 and 2005 respectively.[61, 62] In 2003 the Dutch version of the UDI was validated by van der Vaart et al.[63] This resulted in the first Dutch standard urogynecological questionnaire approved by the Dutch Pelvic Floor Society of Gynecologists *(Werkgroep Bekkenbodem-NVOG)*, released for use by 'urogynecologists' in 2006. This standard questionnaire is a comprehensive summary of in total 47 questions, among which 42 concern urinary incontinence (UDI derived), genital prolapse and defecatory disorders (Defecatory Distress Inventory), and the impact of these disorders on several quality of life domains (Incontinence Impact Questionnaire). The questionnaire has five additional questions on sexual function and also contains an internationally recognized measure of general Health Status, Euroquol-5D (EQ5-D) and in the 'follow-up version' a Patient Global Impression of Improvement scale (PGI-I).[64-66] This widely used Dutch questionnaire is divided in 3 subcategories (UDI, DDI and IIQ), of which each is subdivided in domains (5 for the UDI, 4 for the DDI and 5 for the IIQ), with a score ranging from 0 to 100, whereby

low scores indicate little bother and good quality of life and high scores the reverse: lots of symptom bother and worst quality of life.

III. Sexual Function questionnaire

Although the Standard Dutch Urogynecological Questionnaire contains a few questions on sexual function, these are not exclusively informative. On the other hand, two international widely used sexual function questionnaires are available. The Female Sexual Function Index (FSFI), developed by Rosen et al in 2000 is one of these.[67] This questionnaire however is a generic one and was not developed to be condition specific for women with pelvic floor disorders. In 2001 therefore Rogers et al developed a condition-specific, validated, and self administered questionnaire to evaluate sexual function in women with POP and/or UI (PISQ-31), of which the validated version of the short form, the 'Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire' short form (PISQ-12), is the other and was published in 2003.[68, 69]

The PISQ-12 has been translated into Dutch. Forward and backward translation by native speakers and a panel discussion with experts in the field has been performed. From that time onwards the Dutch translated version of the PISQ-12 has been supplemented to the Standard Urogynecological Questionnaire of the 'Werkgroep Bekkenbodem-NVOG'.

SOURCE

In 2005 the Reinier de Graaf Group Delft/Voorburg and the Radboud University Medical Center decided to start a collaborative database, in which the data of all consecutive prolapse patients from these two urogynecological centers were stored and saved for the sake of scientific research. This still growing database is the principal and basic source of the studies presented in this thesis. The outcomes of these studies however, serve more goals than mere academic research. They are an excellent means of clinical evaluation of the various surgical prolapse procedures performed in these two cooperating urogynecological centers.

OUTLINE OF THIS THESIS

This thesis studies the anatomic and functional outcomes of vaginal prolapse repair techniques, with and without the use of a synthetic mesh.
The main research questions were the following:

- What are the anatomical and functional outcomes of midline fascial plication under continuous digital transrectal control for the repair of posterior vaginal wall prolapse? (Chapter 2)
- Can we identify factors that are responsible for anatomic failure of this midline fascial plication? (Chapter 2)
- Is the use of titanium coated ultra light-weight synthetic mesh safe, when used for augmentation of traditional colporrhaphies in patients with a recurrent prolapse stage ≥ II or a primary prolapse stage ≥ III, and what are the anatomical and functional outcomes? (Chapter 3)
- Is a total trocar-guided tension free vaginal mesh repair with one continuous piece of synthetic polypropylene mesh safe, and what are the anatomical and functional outcomes of such a repair in patients with a post-hysterectomy vaginal wall prolapse? (Chapter 4)
- What are the anatomical outcomes of a partially absorbable lightweight polypropylene mesh and are these comparable to the original non-absorbable mesh in patients with a pelvic organ prolapse stage ≥ III? (Chapter 5)
- How is sexual function affected in patients who are surgically treated with a partially absorbable synthetic mesh for pelvic organ prolapse stage ≥ III? (Chapter 5)
- Is sexual function affected differently in patients with recurrent prolapse who are treated surgically either with trocar-guided mesh insertion or by a native tissue repair? (Chapter 6)
- Can we identify factors that are associated with deterioration in sexual function? (Chapter 6)
- What are the anatomic results of trocar-guided tension free vaginal mesh insertion according different outcome definitions? (Chapter 7)
- Can we identify predictors of failure in trocar-guided tension free vaginal mesh surgery? (Chapter 7)

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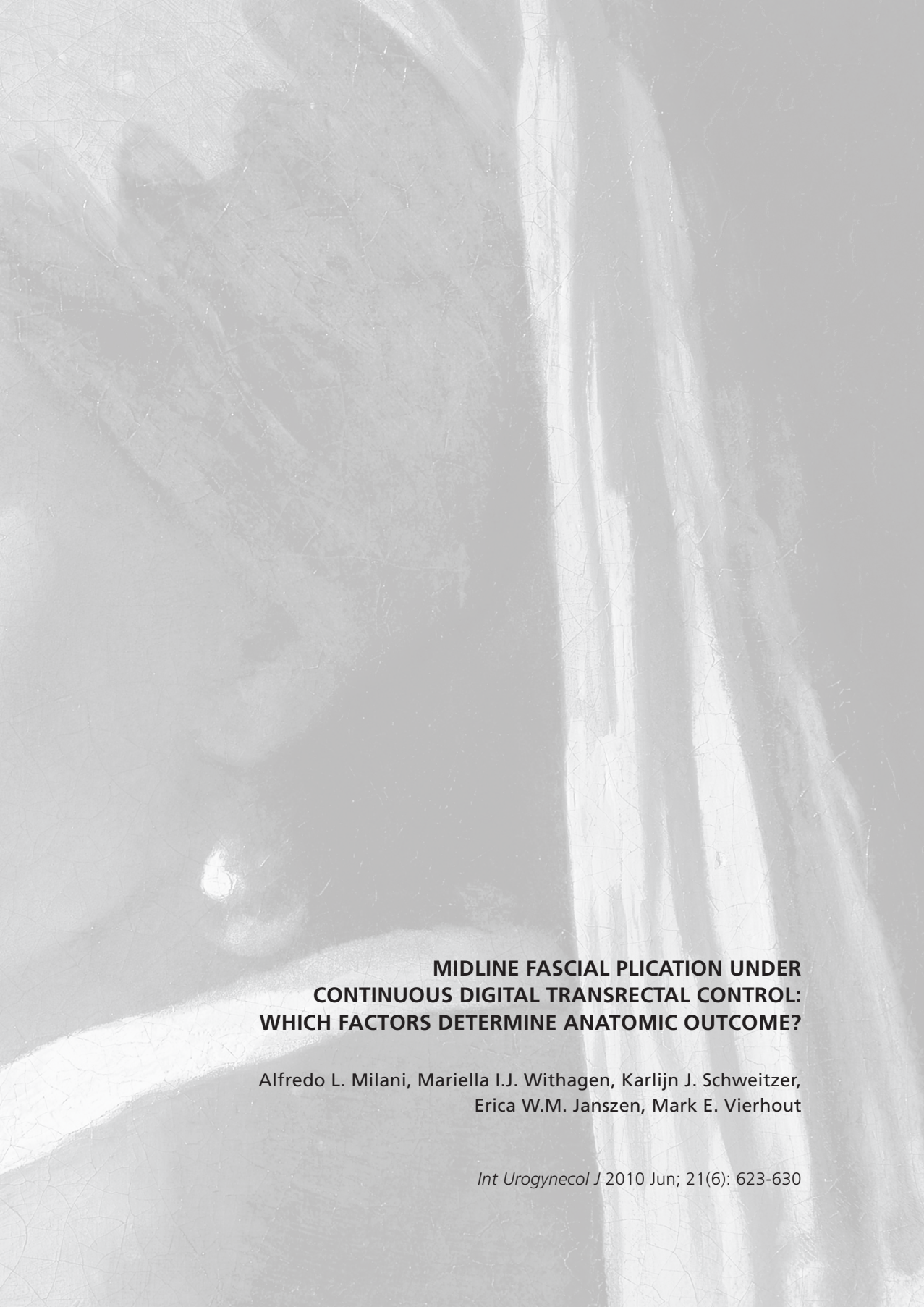

MIDLINE FASCIAL PLICATION UNDER CONTINUOUS DIGITAL TRANSRECTAL CONTROL: WHICH FACTORS DETERMINE ANATOMIC OUTCOME?

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ABSTRACT

Introduction and hypothesis

The aim of the study was to report anatomic and functional outcome of midline fascial plication under continuous digital transrectal control and to identify predictors of anatomic failure.

Methods

Prospective observational cohort study. Anatomic success defined as POP-Q stage ≤ I of the posterior compartment. Validated questionnaires to measure bother and impact on quality of life. Logistic regression was used to identify risk factors for anatomic failure.

Results

Two hundred thirty-three patients with posterior POP stage ≥ II underwent midline fascial plication under continuous digital transrectal control. Median follow-up: 14 months (12-35), and anatomic success was 80.3% (95% CI 75-86). Independent predictors of failure were posterior compartment POP stage ≥ III [OR 8.7 (95% CI 2.7--28.1)] and prior colposuspension [OR 5.6 (95% CI 1.1 – 27.8)]. Sixty-three percent of patients bothered by obstructed defaecation experienced relief after surgery.

Conclusions

Anatomic and functional outcomes were good. Risk factors for anatomic failure were initial size of posterior POP (stage ≥ III) and prior colposuspension.

INTRODUCTION

Posterior colporrhaphy is reported to be one of the most common gynaecological procedures performed in over 40% of women undergoing surgical correction of prolapse.[1]

Restoration of the posterior compartment, which includes perineum, rectum and the peritoneum of the cul-de-sac, knows many approaches. The transvaginal, transanal and laparoscopic approaches have been described to correct defects in this compartment.[2]

In a randomized controlled trial that compared the transanal with the transvaginal approach, the latter approach proved to be anatomically more successful.[3] Maher et al. have demonstrated excellent anatomic and functional outcomes after midline rectovaginal fascial plication.[4] In a retrospective survey by Abramov et al. a significant higher anatomic recurrence rate of rectoceles was noted after discrete site-specific repair as compared to the midline fascial plication.[5] Therefore at present the midline plication of rectovaginal connective tissue is considered to be the most suitable surgical approach for the repair of symptomatic posterior vaginal wall prolapse.

We have added an, in our opinion, important element of the discrete fascial defect repair to our surgical protocol of midline fascial plication, namely the continuous digital transrectal control with the index finger of the non dominant hand.[6]

In the majority of women pelvic organ support defects rarely exist in only one vaginal compartment; in a population based sample of women with POP, the most frequent single compartment affected was the posterior wall, where isolated prolapse was seen in 20% of women, but the most common prolapse combination was anterior and posterior wall in 40%.[7] Therefore combined surgical procedures will often have to be performed to correct these defects. The influence of concomitant POP surgery on the anatomic outcome in the posterior compartment has not received much attention in the literature.[8]

The aim of this article is twofold: to report the anatomical and functional outcome of midline fascial plication under continuous digital transrectal control and to identify independent risk factors for anatomic failure in the posterior compartment.

MATERIAL AND METHODS

In 2003 we started a prospective data registry of all patients undergoing POP surgery in two major urogynecological centres in the Netherlands, the Reinier de Graaf Hospital in Delft and the Radboud University Medical Centre in Nijmegen. After obtaining informed consent consecutive patients were enrolled in this prospective observational cohort registry.

Preoperatively genital prolapse was quantified in the dorsal lithotomy position using the POP-Q measurement system, as recommended by the ICS.[9] Patients were asked to complete the standard urogynecological questionnaire of the Dutch Pelvic Floor Society.

This questionnaire contains the validated Dutch versions of the Urinary Distress Inventory (UDI), the Incontinence Impact Questionnaire (IIQ) and the Defaecatory Distress Inventory (DDI).[10-12] The questionnaire contains some questions on sexual

functioning as well. Patients rate the amount of bother in various domains on a 5-point Likert scale, ranging from 0 (no bother at all) to 4 (a lot of bother). Domain scores for UDI, DDI and IIQ are calculated and range from 0 (no bother at all or best quality of life) to100 (most bother or worst quality of life). Patients were considered to be significantly bothered in any of the DDI domains if the average answer to the questions of that particular domain was at least a little bother (to a lot), which was equivalent to a domain score of ≥ 33 (range 0-100).

Surgical procedure

Peroperative antibiotic prophylaxis was given with a single dose of Cefalozine--Natrium (Kefzol® Lilly, the Netherlands) and Metronidazol (Flagyl® Aventis Pharma BV Hoevelaken, the Netherlands). Patients were positioned in the dorsal lithotomy position with their hips flexed between 90° and 110°. After hydrodissection (Lidocaine hydrochloride monohydrate 200mg with epinephrine hydrogen tartrate100µ g in 20 ml - Astra Zeneca BV Zoetermeer the Netherlands- diluted in 100 ml of 0.9% saline solution) a midline incision was made in the posterior vaginal wall from an area at least 1cm above the superior aspect of the vaginal defect close to the posterior fornix all the way to the level of the posterior fourchette. The incision was not as deep as is used in mesh surgery, but at a more superficial level to allow identification of the so called rectovaginal 'fascia', achieved by cleaving the vaginal wall at the level of its fibromuscular and adventitial layer. Allis clamps were placed on the vaginal walls and usually gentle sideward traction produced a nice cleavage area. A gloved finger covered with an unwound gauze helped further blunt dissection when considered necessary. The gloved index finger of the non-dominant hand was then introduced into the rectum and with the finger and thumb of this hand connective tissue could be grasped on both lateral sides to allow placement of several interrupted Vicryl 2-0 sutures. More cranially the connective tissue layer is less apparent and at these points a thin layer of the adventitia and fibromuscular vaginal wall was grasped bilaterally to be incorporated in the sutures.[13] Plication of the fascia was performed in a cranial--caudal direction with an average number of 6- 8 sutures. Knots of the sutures were tied by the assistant under continuous control by the non-dominant finger of the surgeon. On removal of the finger from the rectum, gloves were changed and modest vaginal trimming was performed bilaterally. A running Vicryl 2-0 suture was used to close the vaginal wall from cranial to caudal direction (fig 1 a-h). A gauze pack was left overnight in the vagina as well as an indwelling urinary catheter. Patients were all operated by or under supervision of the first or last author. The other authors performed surgery after being trained by the former.

Study endpoints

Primary endpoints of this study were anatomic outcome of the posterior compartment after a follow up period of at least 12 months and the identification of independent predictors of anatomic failure. Secondary endpoints were functional efficacy in terms of significant change in experienced bother in the various domains of UDI, DDI and IIQ, as well as effect of surgery on dyspareunia.

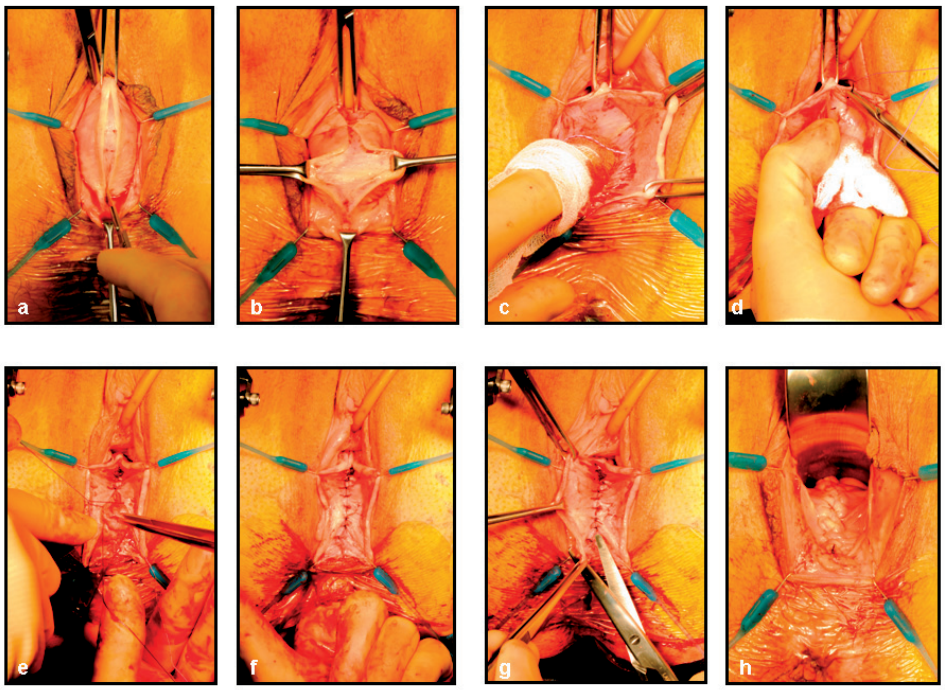

Figure 1. Midline fascial plication under continuous transrectal control of a stage II posterior vaginal wall prolapse. a. Incision after hydrodissection. b. Sideward traction and cleavage of vaginal wall. c. Blunt dissection of fascia. d. Suturing at cranial side of rectocele. e. Tie of a knot by the assistant of the surgeon. f. Transrectal control of firmness. g. Trimming of vaginal wall. h. End result and running suture of vaginal wall.

Anatomic success was defined as ICS POP stage 0 or I of the posterior compartment. Anatomic failure as a POP stage ≥ II of the posterior compartment.[9] Follow-up investigations were performed, by the second, third and fourth author.

Data collection

To obtain data on anatomical efficacy POP-Q measurements at baseline were compared with those obtained at follow up. Data on the functional efficacy, quality of life and effect on sexual function were derived from the standard urogynecological questionnaires at baseline and follow-up. Data were analysed using a Statistical Package for the Social Sciences 17.0 database.

Baseline and surgical data are presented as median (range) or numbers with corresponding percentages and where appropriate with 95% Confidence Intervals. Pearson's Chi square was used where appropriate. Domain scores of UDI, DDI and IIQ are presented as means with standard deviations. Differences in means between baseline and follow-up were tested with the paired-samples t-test. A p-value ≤0.05 was considered significant. To quantify clinically relevant effects, effect sizes were calculated in the various domains of UDI, DDI and IIQ by using Cohen's d, which

represents the difference between two means divided by the pooled standard deviations of these means. The effect size is defined as small if Cohen's d = 0.2, medium if d = 0.5 and large if d ≥ 0.8.[14]

Univariable logistic analysis was performed to select potential risk factors for anatomic failure. Covariables that showed a p value <0.1 at univariable analysis were entered in a stepwise forward multivariable logistic regression model to identify independent predictors of anatomic failure. P-values < 0.05 were considered significant and data are presented as adjusted odds ratio with 95% confidence intervals.

RESULTS

Two hundred and thirty-three patients with a posterior vaginal wall prolapse stage II or more were operated and available for follow-up analysis. Median follow-up was 14 (12-35) months. Not all patients responded to our invitation for follow-up examination, but on 208 (89%) patients a POP-Q examination could be performed. At baseline one hundred and eighty-seven (80%) and at follow-up two hundred and fourteen patients (92%) responded to our request to complete the urogynecological questionnaire.

Baseline and surgical characteristics are presented in table 1. Seventy-three patients (31%) underwent an isolated posterior wall repair procedure; all others (69%) underwent concomitant repairs in the other vaginal compartments as well.

Anatomical results

Data on POP-Q measurements and POP stage at baseline and follow-up are shown in table 2. Overall anatomic success in the posterior compartment was 80% (95% CI 75-86). Sub analysis revealed a success rate of 85 % (95% CI 79-91) for combined posterior repairs and 70% (95% CI 59-81) for isolated repairs.

Predictors of failure

Table 3 shows the results of univariable and multivariable analysis of covariates potentially related to anatomic failure. Five covariates were entered in a stepwise forward multivariate logistic analysis model. Posterior POP stage ≥ III and a history of prior colposuspension were the only factors that could be identified as independent significant predictors of anatomic failure in the posterior compartment.

Functional results

Functional data on the various domains of UDI, DDI and IIQ with their respective calculated effect sizes are summarized in table 4. Except for fecal incontinence all domains of UDI, DDI and IIQ showed statistically significant improvements. The domains of genital prolapse and pain in the UDI revealed a large treatment effect size (Cohen's d ≥ 0.8). For all DDI domains, effect sizes appeared to be of medium size only (0.3-0.7).

At baseline 150 patients completed all questions in the domain of obstructed defaecation. Thirty-eight (25%) were considered to be significantly bothered (domain score ≥ 33). Mean domain score before surgery of these patients was 48.5 (SD16.9).

Table 1. Baseline and surgical characteristics.

	N: 233
Age (years)	59 (29-85)
BMI (kg/m^2)	25 (16-42)
Parity	2 (1-10)
Postmenopausal	180 (77%)
Prior related surgery	
Vaginal hysterectomy	77 (33%)
Abdominal hysterectomy	39 (17%)
Anterior colporrhaphy	51 (22%)
Posterior colporrhaphy	44 (19%)
Sacrocolpopexy	12 (5%)
2 prior prolapse repairs	21 (9%)
≥3 prior prolapse repairs	24 (10%)
Prior incontinence surgery	
Colposuspension	34 (15%)
TVT	8 (3%)
Surgical procedures	
Isolated posterior repair	73 (31%)
Combined repairs	160 (69%)
Anterior colporrhaphy	143 (89%)
Perineoplasty	38 (24%)
Manchester procedure	28 (17%)
Vaginal hysterectomy	43 (27%)
McCall & enteroceleplasty	22 (14%)
Surgical characteristics	
Duration of surgery (min)	75 (10-205)
Bloodloss (ml)	100 (40-600)
Spinal analgesia	104 (45%)
General anesthesia	129 (55%)
Hospital stay (days)	4 (2-13)

Data presented as median (range) or number (percentages).

Mean postoperative score was 22.5 (SD17.2) ($p<0.001$, effect size: 1.5). Twenty-four patients (63%) reported to be cured or improved at follow-up.

At baseline 170 of the 187 patients who completed the urogynecological questionnaire answered questions on sexual functioning. Hundred and ten patients (65%) reported to be sexually active. At follow-up this percentage remained unchanged: 64%. At baseline 42% of patients reported to have some degree of dyspareunia. At follow-up this rate had dropped to 34%. Nineteen percent of patients who did not complain of dyspareunia before surgery reported this complaint at follow-up, so this was considered to be de novo dyspareunia. Fifty-eight percent of patients however, who initially complained of dyspareunia, reported to be cured at follow-up.

Table 2. POP-stage and POP-Q variables at baseline and follow-up.

POP-Q variable		Baseline (233)		Follow-up (208)		Change from baseline
Ba		0.2 (2.2)		-1.5 (1.5)		1.7 (2.2)
C		-4.2 (3.4)		-6.7 (2.3)		2.5 (4.1)
D		-5.2 (3.3)		-7.8 (2.2)		1.4 (4.0)
Bp		0.5 (1.2)		-2.2 (1.2)		2.7 (1.3)
TVL		9.4 (1.5)		9.1 (0.9)		0.3 (1.6)
GH		4.6 (1.1)		3.7 (0.9)		0.8 (1.2)
PB		3.4 (1.2)		3.8 (1.0)		0.4 (1.4)
POP stage						**Success rate**
Anterior	0	26 (11.1%)		63 (30.3%)		
	I	40 (17.2%)		65 (31.2%)		
	II	98 (42.1%)		75 (36.1%)		61.5% (54.4-67.7)
	III	69 (29.6%)		5 (2.4%)		
	IV	-		-		
Apical	0	55 (23.6%)		87 (41.8%)		
	I	142 (60.9%)		116 (55.8%)		
	II	17 (7.3%)		1 (0.5%)		97.6% (95.5-99.7)
	III	19 (8.2%)		4 (1.9%)		
	IV	-		-		
Posterior		*Isolated*	*Combined*	*Isolated*	*Combined*	
	0	-	-	27 (40.3%)	80 (56.7%)	
	I	-	-	20 (29.8%)	40 (28.4%)	**80.3% (74.9-85.7)†**
	II	43 (58.9%)	136 (85%)	17 (25.4%)	21 (14.9%)	
	III	30 (41.1%)‡	24 (15%)‡	3 (4.5%)	-	
	IV	-	-	-	-	

Data are presented as mean (± standard deviation) cm for POP-Q variable and as number of patients (percentage) for POP stage.
Ba: most descendant point at anterior vaginal wall. C: vaginal apex. Bp: most descendant point at posterior vaginal wall (all in cm distance from the hymenal remnants).
TVL: Total Vaginal Length, GH: Genital Hiatus, PB: Perineal Body length in cm (± standard deviation).
† 95% Confidence Interval. ‡ Pearson's Chi square: $p < 0.001$.

DISCUSSION

The surgical technique used by us actually is a combination of the classical midline *fascial* plication and a site defect specific repair. The addition of continuous transrectal digital control during the procedure helps identify any interruptions in the connective tissue layers and one ensures that the repair is sufficiently solid, has no weak spots and that no sutures accidentally enter the rectal lumen. A relative disadvantage of our technique though, is the fact that the surgeon cannot tie the sutures himself but has to rely on the assistant for this. Whether this protocol assignment significantly contributes to the anatomical efficacy is not shown by our study but can only be determined in a controlled study that compares the 'classical' midline plication with a procedure that adds this 'continuous transrectal control'.

Table 3. Univariable and multivariable logistic regression analysis of factors that might influence anatomic outcome.

	Univariable analysis		Multivariable analysis	
Covariables	**p**	**OR (95% CI)**	**p**	**OR (95% CI)**
Age	0.089	1.026 (0.996 – 1.058)	0.409	
Prior posterior wall repair	0.243	0.292 (0.037 – 2.302)		
Prior sacrocolpopexy	0.602	0.563 (0.065 – 4.877)		
Prior POP surgery	0.068	1.917 (0.954 – 3.851)	0.529	
Prior colposuspension	0.062	3.893 (0.934 – 16.226)	**0.037**	5.558 (1.112 – 27.779)
Isolated posterior repairs	**0.013**	2.432 (1.209 – 4.892)	0.124	
Concomitant anterior colporrhaphy	0.439	0.711 (0.934 – 16.226)		
Concomitant apical support surgery	0.774	0.882 (0.375 – 2.076)		
Concomitant perineoplasty	0.198	0.497 (0.171 – 1.440)		
Concomitant vaginal hysterectomy	0.300	0.586 (0.213 – 1.611)		
Posterior compartment stage ≥ III	**<0.001**	7.613 (3.585 – 16.170)	**<0.001**	8.767 (2.739 – 28.060)

Data presented with p-values and odds ratio's (OR) with 95% CI.
Covariables with $p < 0.1$ in univariable analysis (n: 5) were entered in a multivariable logistic analysis model, method stepwise forward (LR).
Significant p values are shown in **bold**.

Anatomical results and risk factors for failure

The overall anatomic cure rate of 80% (95% CI 75-86) is comparable with previous reports on midline fascial plication by other authors, though our study group was considerably larger.[4, 5, 15, 16]

Only two factors, POP-Q stage > II in the posterior compartment and a history of prior colposuspension, were identified as independent risk factors. Two other authors demonstrated already earlier that women with POP stage ≥ III are at increased risk of developing a recurrence or failure after surgical repair without grafts.[17, 18] Prior colposuspension is known to provoke posterior compartment prolapse, but has never been identified as a risk factor for recurrence after posterior compartment surgery.[19]

An interesting finding was the fact that at first glance the anatomical outcome of patients with combined repairs appeared significantly better than the outcome after isolated repairs only. In the isolated repair group though a significantly higher percentage of patients with a posterior POP stage III were present as compared to the combined repairs (table 2). In the group that underwent concomitant repairs, DeLancey's level I support was taken care of, as by the modified Manchester procedure or high McCall procedure, in 50 of 160 patients (31%; Table1).[20, 21] It has been reported that apical support might explain half of the variation in anterior compartment support.[22] To a somewhat lesser extent this could be demonstrated for the posterior compartment as well; in a group of patients with POP stage ≥ II Lowder et al demonstrated that point Bp changed to stage 0 and I after simulated apical support in at least 30% of cases.[8] In our study though, we could not detect

Table 4. UDI, DDI and IIQ domain scores at baseline and follow-up with calculated effect sizes.

Domains UDI	Baseline (187)	Follow-up (214)	P*	Effect Size†
Prolapse	45.1 (33.0)	7.7 (18.5)	< 0.001	2.9
Incontinence	26.5 (26.1)	20.9 (23.7)	< 0.001	0.5
Overactive bladder	31.7 (24.9)	22.9 (23.2)	< 0.001	0.7
Obstructive micturition	25.8 (26.9)	17.7 (23.0)	< 0.001	0.6
Pain	33.7 (29.3)	18.1 (23.0)	< 0.001	**1.2**
Domains DDI				
Constipation	16.8 (20.4)	12.2 (19.3)	0.002	0.4
Obstructed defaecation	17.5 (20.6)	11.2 (15.1)	< 0.001	0.7
Pain	14.6 (23.0)	10.1 (20.0)	0.014	0.4
Incontinence	7.1 (16.0)	5.8 (14.2)	0.065	0.3
Domains IIQ				
Physical functioning	27.6 (28.3)	16.2 (27.2)	< 0.001	**0.8**
Mobility	33.0 (25.7)	22.3 (24.8)	< 0.001	**0.8**
Emotional health	27.1 (26.3)	17.9 (24.5)	< 0.001	0.7
Social functioning	16.1 (18.3)	12.0 (19.3)	< 0.001	0.4
Embarrassment	15.0 (20.4)	12.2 (21.6)	0.005	0.3

UDI: Urinary Distress Inventory, DDI: Defaecatory Distress Inventory, IIQ: Incontinence Impact Questionnaire.
Scores presented as mean (± standard deviation). Scores range between 0 (least bother and best quality of life) to 100 (maximum bother and worst quality of life).
P* Paired samples t-test. †Effect size (Cohen's d): Small: 0.2; Medium 0.5; Large ≥ 0.8 (in **bold**).

any significant protective effect of the above mentioned apical support surgery on the anatomic outcome in the posterior compartment.

The vast majority of patients that underwent concomitant surgery underwent an anterior colporrhaphy as well (89%). The success rate of the group as a whole in the anterior compartment was 61.5% (54.4-67.7) (table 2). Although the outcome in the anterior compartment was not an endpoint in this study, results are half as good as compared to the posterior compartment, but comparable with recent reports by other authors.[23, 24] Concomitant anterior repairs did not influence outcome of the posterior compartment.

Although in our study prior prolapse repair surgery as a whole appeared close to significance at univariable analysis, neither this factor nor a prior posterior wall repair could be identified as significant risk factor for anatomic failure of the posterior compartment.

Functional results

All mean domain scores of the UDI show statistically significant improvements, of which two domains even with a large effect size, of which the domain of genital prolapse shows the largest calculated effect size at follow up. Except for the domain of faecal incontinence, all domains of the DDI show statistically significant improvements as well, however with a smaller effect size. Although only weak correlations between bowel symptoms and posterior vaginal wall prolapse have been reported, the defaecatory

symptom that most consistently arose with respect to posterior vaginal prolapse, was the need to splint the vagina or perineum to defaecate.[25] Thus we were especially interested in the domain of obstructed defaecation. Seventy-five percent of patients were not considered to be significantly bothered by obstructed defaecation. That means that mean domain scores of the group as a whole were dampened by those who are not bothered at all, which is demonstrated by the low initial score. However, if patients were significantly bothered by obstructed defaecation, the improvement in this domain score appeared not only statistically significant, but also demonstrated a large effect size. In our study patients that were significantly bothered by obstructed defaecation had a 63% chance that these symptoms improved or disappeared after surgery.

The positive effects of surgery on the quality of life of patients are particularly demonstrated for the domains of physical functioning and patients' mobility.

The percentage of patients that reported dyspareunia had decreased at follow-up. Though19% of patients reported de novo dyspareunia, in 58% this complaint was no longer present after surgery. We realize that this section of the urogynecological questionnaire is rather intimate for most (older) patients and therefore the least well answered part. However, the data are comparable with data published by other authors and earlier work by us.[4, 15, 16, 26, 27]

Strengths and weaknesses

Strengths of this study are the large sample size with a high follow-up rate and the use of validated instruments as recommended by the ICS, such as POP-Q and validated urogynecological questionnaires. Another strength is the systematic surgical protocol followed by all surgeons.

Drawbacks however are, that at the start of our registry we missed some questionnaires, so that the number of questionnaires at follow-up was somewhat higher than at baseline. The tendency of our, mostly older, patients to be somewhat reluctant with the response to questions on sexual functioning is another concern that deserves an appropriate solution for the benefit of future research.

CONCLUSION

Midline 'fascial' plication under continuous digital transrectal control for the repair of symptomatic posterior vaginal wall prolapse is anatomically and functionally effective.

Two independent risk factors for anatomic failure could be identified: POP stage ≥ III of the posterior compartment and a history of prior colposuspension.

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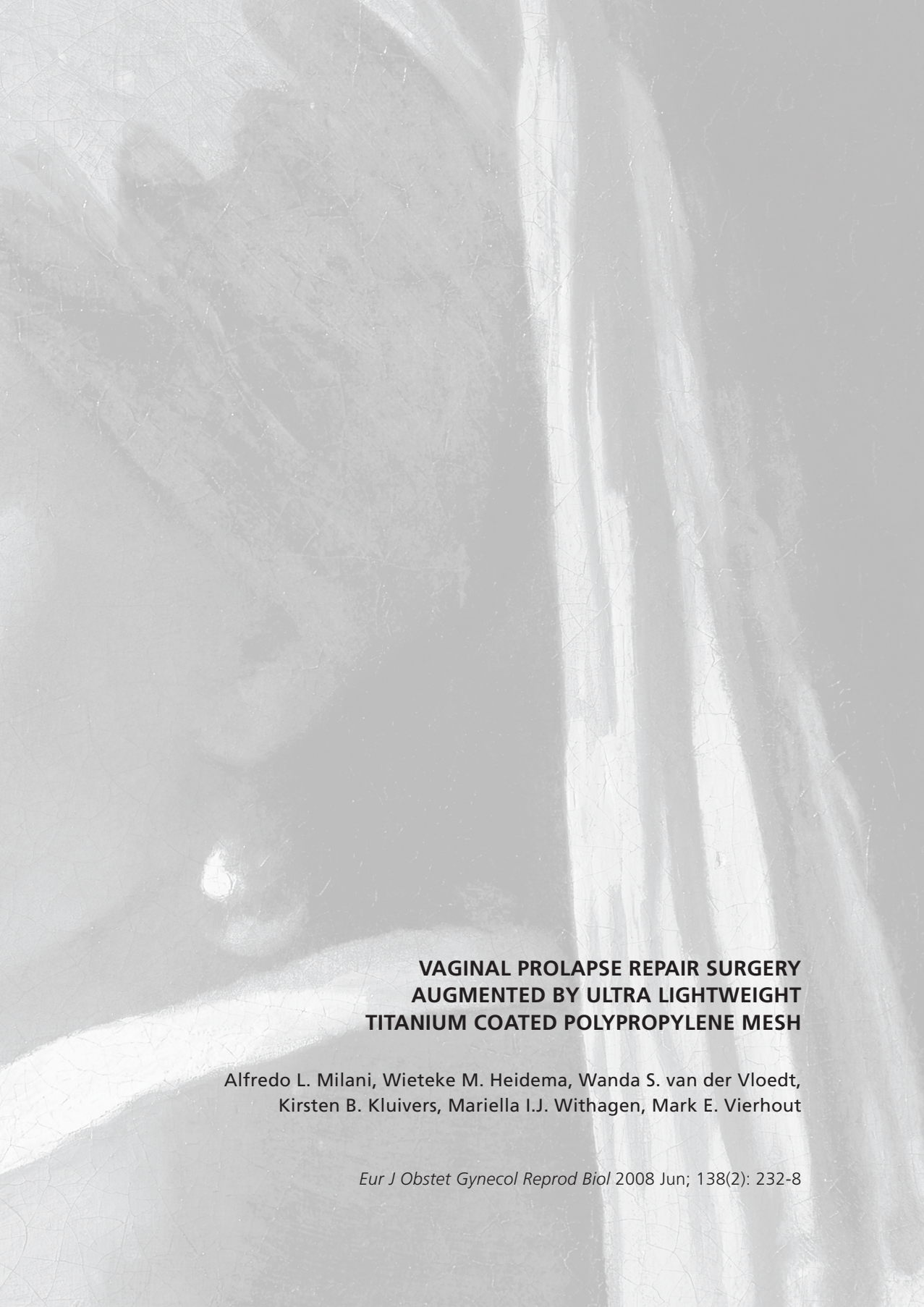

VAGINAL PROLAPSE REPAIR SURGERY AUGMENTED BY ULTRA LIGHTWEIGHT TITANIUM COATED POLYPROPYLENE MESH

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ABSTRACT

Objectives

To determine the safety and efficacy of ultra lightweight titanium coated polypropylene mesh to augment conventional vaginal prolapse repair in women with recurrent symptomatic prolapse stage II or more or primary prolapse stage III or more.

Study design

A prospective observational cohort study was performed at two urogynecological centres in the Netherlands. Women with recurrent symptomatic prolapse at least stage II or primary vaginal prolapse ICS POP stage III or more participated in the study. POP-Q and validated urogynecological questionnaires were used pre- and postoperatively. Outcome measures were mesh-related morbidity and prolapse recurrence, defined as ICS POP stage II, as well as changes in domain scores on Urogenital Distress- and Defaecatory Distress Inventory (UDI and DDI), Incontinence Impact Questionnaire (IIQ) as well as sexual functioning. Wilcoxon's signed ranks test for paired variables and 95% confidence intervals, respectively were used to analyse these data.

Results

The study group comprised 71 patients with a median follow-up of 9 months (6-14).

Mesh erosions were detected in four patients (5.6%), all on the posterior vaginal wall. After Ti-mesh® augmentation in 14 patients (36%) the anterior vaginal wall and in 7 patients (18%) the posterior vaginal wall, was categorised as ICS POP stage II and were thus considered failures. UDI and DDI domain scores all improved significantly, except for the domains of incontinence and pain, respectively. Three out of five domains of the IIQ showed significant improvement. Surgery did not have any significant negative impact on sexual functioning.

Conclusion

Ultra lightweight titanized polypropylene mesh to augment conventional vaginal prolapse repair surgery showed minimal morbidity, but no additional value compared to conventional surgery at short-term follow-up.

INTRODUCTION

Pelvic Organ Prolapse (POP) is a highly prevalent condition among the ageing female population.[1] Olsen et al. calculated that by the age of 80 years 11.1% will have undergone a single operation for prolapse or incontinence (lifetime risk). Reoperation was found to be common (29.2%) and the interval between repeat procedures decreased with each successive repair.[2] Between 2000 and 2003, the number of operations performed annually for POP in the Netherlands increased by almost 16%.[3] Prolapse recurrence after vaginal prolapse repair surgery occurs frequently: in 26% to 34% of anterior wall repairs and in about 12% of posterior wall repairs.[4, 5] Recurrences after surgical repair were more common in women who prolapsed at a younger age and in women with more advanced stages of POP.[6] The reason for the growing interest in biocompatible synthetic meshes to augment prolapse repair surgery lies within the need to reduce the high recurrence rates of vaginal prolapse. In inguinal and femoral hernia surgery, there is distinct evidence that the use of synthetic mesh to augment repair surgery considerably reduces the risk of recurrence.[7] Unfortunately, the use of such mesh in vaginal prolapse repair surgery is relatively contraindicated, because various complications can arise, such as rejection, tissue erosion and shrinkage. The ideal synthetic mesh is type I, macroporous monofilament polypropylene.[8] Several studies showed advantages of the addition of polypropylene mesh in vaginal prolapse repair surgery.[9-11] However only in two studies polypropylene mesh was used to augment traditional colporrhaphy.[12,13] In one of these publications, the authors advised against the use of Prolene mesh in vaginal prolapse repair surgery, because of the high rates of postoperative dyspareunia and erosions.[13] In an animal (rat) experiment it could be shown that lightweight polypropylene mesh had more favourable biocompatible characteristics than the conventional heavyweight polypropylene mesh, without losing any critical tensile strength.[14] In another animal (pig) study different types of polypropylene mesh and their handling properties were compared and was found that coating the mesh with titanium caused less severe inflammatory reactions than non-coated polypropylene. This titanium coated mesh (Ti-Mesh®) combined the advantages of material reduced polypropylene with a superior biocompatibility of a titanium coating, at least in terms of chronic inflammatory reactions.[15]

Ti-Mesh® *(GfE Medizintechnik GmbH, Höfener Strasse 45, 90431, Nürnberg, Germany)* is commercially available in two variants: a lightweight (35 gr/m^2) and an ultra lightweight variant (16 gr/m^2). The layer of titanium coating is only 30 nm. Preliminary results after its use in human inguinal hernia surgery were good.[16]

We performed a prospective observational pilot study on this new ultra lightweight titanium coated mesh in human vaginal prolapse repair surgery. The aim of the study was to establish material safety, in terms of mesh related morbidity, and its efficacy, in terms of prolapse recurrence, bother and health related quality of life. The mesh was used in conventional vaginal prolapse repair for patients with recurrent symptomatic prolapse ICS stage II or more, or primary vaginal prolapse stage III or more.

MATERIALS AND METHODS

The sample size was calculated for bother as measured by the domain genital prolapse in the UDI. A difference of 20 units per scale was considered as a clinical relevant treatment related change. With standard deviation of 40 units, a type I error of 0,05 and 90% power, 44 patients were needed using a two-sided paired t-test. We estimated, prior to the start of this prospective observational study, that a recruitment period of 18 months would be needed to include these patients in two centres.

Between June 2004 and November 2005, 78 women with recurrent symptomatic prolapse or primary vaginal prolapse ICS stage III or more were operated on and asked to participate. All the participants gave written informed consent. The study was performed at two centres: the Reinier de Graaf Hospital, Delft-Voorburg and the St. Radboud University Medical Centre, Nijmegen.

Genital prolapse was quantified pre- and postoperatively in the dorsal lithotomy position according to the POP-Q system, as recommended by the ICS.[17] In this system the most distal part of the prolapsed upper anterior vaginal wall is called point Ba and that of the posterior vaginal wall point Bp. Their distance is measured in centimetres to the hymenal remnants. A negative value indicates that the most dependant part of prolapse is located within the hymenal remnants, whereas a positive value means prolapse beyond the hymen.

The standard urogynecological questionnaire (proposed by the Pelvic Floor Committee of the Dutch Gynaecological Society) was completed before and after surgery. This questionnaire includes questions that address the general quality of life and health, derived from the Dutch version of the Euroqol 5D.[18] Disease-specific questions on quality of life and bother were incorporated from the validated Dutch translation of the Incontinence Impact Questionnaire and Urogenital Distress Inventory respectively.[19] Questions were also added from the recently validated Defaecatory Distress Inventory (DDI).[20] The more extensive Dutch language standardized version of the questionnaire has been validated as a whole.[21] Several questions addressed sexual functioning.[22] The answers to the questions were transformed into bother scores in the following domains: overactive bladder, obstructed micturition, urinary incontinence, pain and genital prolapse on the UDI and constipation, obstructed defaecation, pain and faecal incontinence on the DDI. Disease-specific quality of life questions covered the following five domains: physical functioning, mobility, emotional and social functioning and embarrassment. Scores could range from 0 (no bother at all or perfect quality of life) to 100 (maximum bother or worst quality of life in a particular domain).

All the operations were performed by the first or last author, or under the direct supervision of one of these. Patients underwent standardized vaginal dissection and subsequent plication of the vesico- or rectovaginal fascia before application of the mesh.

In the case of anterior colporrhaphy (n=41), hydrodissection was performed and 2-3cm distal to the external urethral meatus a midline incision was made to the cervix or vaginal apex. Next, the vaginal mucosa was separated from the

remnants of the vesicovaginal fascia that covers the bladder. These fascial remnants were then plicated with Vicryl 2.0 sutures. In the case of posterior colporrhaphy, a similar hydrodissection and midline incision technique was used, starting from the posterior commisura to the cervix or apex of the vagina. After the rectovaginal fascia was freed, it was plicated in the midline with Vicryl 2.0 sutures under digital control in the rectum by the index finger of the surgeon.[23] To cover the anterior side of the vagina, the mesh was cut into the shape of a long sleeved T shirt. Total width of this graft, including the arms, was approximately 8-9cm. The two arms were brought into the space of Retzius (in the first 20 patients) or introduced through the obturator foramen with the help of a large Deschamps needle. The body of the graft was positioned in such a way that it covered the plicated cystocele. No sutures were used to fix the mesh. To cover the posterior side of the vagina (n=36), the mesh was cut into the shape of a broad V, with two 4-5cm arms at the top. The two arms were inserted into the pararectal space, in the direction of the sacrospinous ligaments. No additional sutures were used to fix the mesh arms. Afterwards the vaginal wall was classically trimmed and closed with a running Vicryl 2.0 suture. All the patients received peroperative antibiotic prophylaxis with Cefazoline- Natrium (*Kefzol® Lilly, the Netherlands*) and Metronidazol (*Flagyl® Aventis Pharma BV Hoevelaken, the Netherlands*).

The first outpatient check-up took place six weeks after surgery and was performed by the surgeon. Special attention was paid to the presence of mesh exposure or other vaginal abnormalities. At follow-up, which was at the earliest six months postoperatively, the above described standard urogynecological questionnaire was readministered to the patients and they were asked to express their satisfaction about the result of the operation on a Visual Analogue Scale (0 = extremely dissatisfied, 10 = extremely satisfied) and invited for anatomical assessment. These examinations were performed by an independent 'non-surgical' resident. Anatomical failure was defined as postoperative POP stage II or more. In five patients, postoperative follow-up was shorter than six months, one patient was unable to comply with our request due to transportation problems and one patient was lost to follow-up. In the remaining 71 patients POP quantification in the dorsal lithotomy position was repeated. The vagina was examined carefully for signs of erosion or mesh-related shrinkage.

All the data were entered into an SPSS database. Mean domain scores were calculated on the UDI, DDI and IIQ. Differences between the preoperative and postoperative scores were tested with Wilcoxon's signed ranks test for paired variables, using SPSS version 12.0.1. Percentages of answers per category and 95% confidence intervals were used to analyse the questions on sexual functioning.

RESULTS

Table 1 shows the baseline patient characteristics and performed surgical procedures. One or more previous prolapse repairs in the same or another compartment had been conducted in the majority (78%) of these patients.

Table 1. Baseline and surgical characteristics

Follow-up in months	9 (6-14)
Age in years	56 (33-78) [a]
BMI in kg/m2	25 (18-41)
Parity	2 (0-7)
Number of previous prolapse surgeries	1 (0-5)
Hospital stay in days	3 (2-7)
Bloodloss in ml	100 (50-600)
Duration of catheterisation in days	3 (1-20)
Number of patients with anterior repair with Ti-mesh	23 (33%) [b]
Posterior repair with Ti-mesh	26 (37%)
Anterior & posterior repair with Ti-mesh	10 (14%)
Anterior repair with Ti-mesh & posterior without	7 (10%)
Anterior repair with Ti-mesh & posterior without & VH[c]	1 (1%)
Posterior repair with Ti-mesh & anterior repair without	3 (5%)

[a] data presented as median (range), [b] data presented as number (percentage), [c] VH= vaginal hysterectomy.

Mesh- related morbidity

In four patients (5.6%) slight 'erosion' of the posterior vaginal wall (size: 2 to 3mm) was detected. All the affected areas were located in the midline at the level of the original vaginal incision. Only one patient had noticed this erosion herself during sexual intercourse. The erosions were treated by simple removal of the piece of exposed mesh and closure of the vaginal defect at the outpatient clinic. None of the patients showed any signs of abnormal consistency, pain on palpation, or changes in the size or shape of the vagina that suggested mesh retraction.

Complications

One patient developed a pararectal haematoma, which was treated conservatively. In one patient, a small part of mesh hung out of the external urethral meatus six weeks after the operation. This bizarre complication had probably been caused by perforation of the bladder peroperatively when the arms of the mesh were introduced into the retropubic space. The piece of mesh could be removed easily by cystoscopy during a day care procedure.

Anatomical results

Changes in mean scores of POP-Q at points Ba and Bp pre- and postoperatively are illustrated in figures 1 and 2. Table 2 (a and b) shows the POP stages before and after surgery with Ti-mesh® augmentation on the anterior wall and posterior wall, respectively. Fourteen patients (36%) who underwent anterior wall repair with Ti-mesh® and seven (18%) who underwent posterior wall repair with Ti-mesh® were postoperatively categorised as POP stage II.

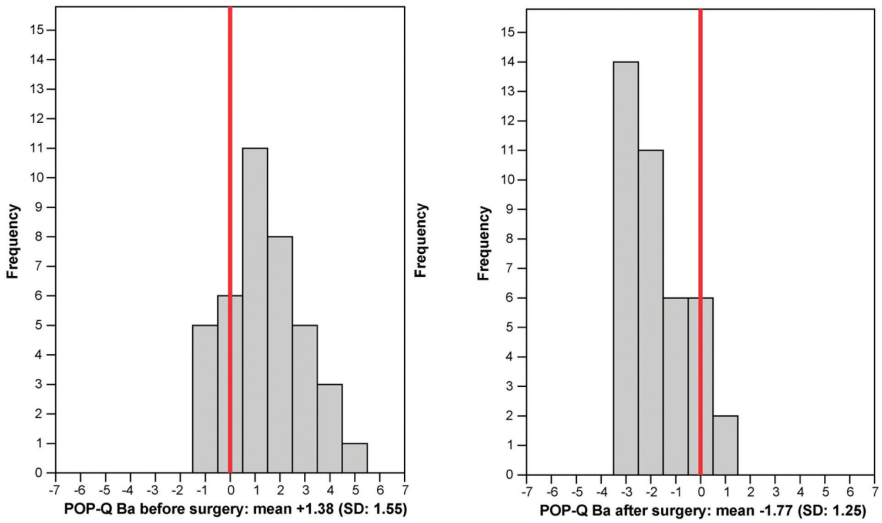

Figure 1. POP-Q point Ba before and after Ti-mesh®.

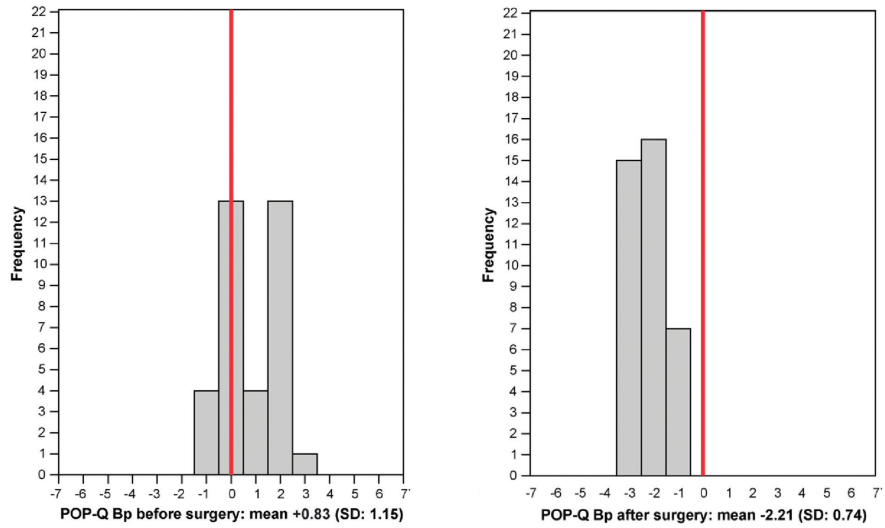

Figure 2. POP-Q point Bp before and after Ti-mesh®.

Functional results

Table 3 shows the mean domain scores on general quality of life, UDI, DDI and IIQ before and after surgery. Scores were significantly lower after prolapse repair, which reflects significant improvements in the various domains, except for general quality of life, urinary incontinence and the domains of social functioning and embarrassment.

Table 2a. Anterior vaginal wall pre- and post-operative ICS POP stages

Anterior vaginal wall	Pre-operative (%)	Post-operative (%)
Stage 0	-	14 (36)
Stage I	-	11 (28)
Stage II	22 (56)	14 (36)
Stage III	17 (44)	-
Stage IV	-	-

Table 2b. Posterior vaginal wall pre- and post-operative ICS POP stages

Posterior vaginal wall	Pre-operative (%)	Post-operative (%)
Stage 0	-	15 (39)
Stage I	-	16 (42)
Stage II	21(60)	7 (18)
Stage III	14 (40)	-
Stage IV	-	-

Table 3. Mean general QoL scores, domain scores on UDI, DDI and IIQ before and after surgery

	Before	After	Difference
General quality of life[a]	6.7 (1.8)	6.9 (1.7)	N.S
UDI Genital Prolapse[b]	56.1 (36.3)	5.2 (10.8)	<0.0001
UDI Incontinence	23.3 (24.6)	25.5 (27.9)	N.S
UDI Overactive Bladder	39.6 (30.0)	31.7 (28.8)	0.003
UDI Obstructive Micturition	34.2 (31.4)	20.3 (23.5)	0.001
UDI Pain	36.7 (31.9)	21.7 (23.4)	<0.0001
DDI Constipation[b]	17.8 (21.0)	10.9 (18.7)	0.002
DDI Obstructed Defecation	22.2 (23.0)	12.5 (14.8)	<0.0001
DDI Incontinence	10.6 (20.3)	5.8 (14.8)	0.038
DDI Pain	14.0 (22.2)	8.3 (18.3)	N.S
IIQ Physical functioning	30.4 (28.5)	21.5 (26.8)	0.049
IIQ mobility	33.7 (26.5)	27.7 (24.2)	0.043
IIQ emotional health	25.0 (26.3)	20.2 (22.5)	0.011
IIQ social functioning	17.0 (20.4)	13.4 (17.4)	N.S
IIQ embarrassment	11.8 (26.3)	14.4 (23.7)	N.S

[a] General QoL scores range 0-10 (SD),
[b] UDI and DDI domains. Scores range 0-100 (SD). 0 reflects no bother at all, 100 maximum bother.
[c] Impact on quality of life domains. Scores range 0-100 (SD). 0= Good quality, 100= worst quality of life.

Table 4 compares the frequency of sexual intercourse and dyspareunia pre- and postoperatively. We could not detect any significant difference in the answers given to these questions before and after prolapse surgery with Ti-mesh® augmentation.

The mean Visual Analogue Scale score for satisfaction with the results of the procedure was 8.13 (± 1.45).

Table 4. Influence of surgery on sexual intercourse and dyspareunia

"How often do you have sexual intercourse?"	**Before surgery**		**After surgery**		
	%	**95% CI**	**%**	**95% CI**	**P**
Answer:					
Never	33	21-45	31	19-42	N.S
< 1 a month	8	1-15	15	7-24	N.S
1-2 times a month	22	11-32	15	7-24	N.S
1 time a week	23	13-34	23	13-33	N.S
Several times a week	13	5-22	15	7-24	N.S
Total (n)	60		65		
"Do you experience pain during sexual intercourse?"	**Before surgery**		**After surgery**		**P**
Answer:					
No, or not at all bothersome	41	29-54	33	22-44	N.S
Yes, a little	12	4-20	16	8-25	N.S
Yes, rather much	19	9-29	15	6-23	N.S
Yes, very much	5	-1-11	9	2-16	N.S
No intercourse	22	12-33	27	16-37	N.S
Total (n)	58		67		
"Is the vagina too narrow to have sexual intercourse?"	**Before surgery**		**After surgery**		**P**
Answer:					
No, or not at all bothersome	73	61-84	65	54-77	N.S
Yes, a little	2	-2-5	0	0-0	N.S
Yes, rather much	2	-2-5	6	0-12	N.S
Yes, very much	2	-2-5	4	0-10	N.S
No intercourse	22	11-33	24	14-35	N.S
Total (n)	59		66		

Data presented as percentages of given answers and 95% confidence intervals.

DISCUSSION

The anatomical results of Ti-mesh augmentation after this short term follow-up are no better then results from previous reports on conventional colporrhaphy alone.[4]

In conformity with others, we defined anatomical failure as POP stage II or more.[24] For the anterior compartment 14 patients (36%) met this criterion. In 4 of them (10%) point Ba had the same value after the operation as before. In all remaining 10 patients point Ba improved (from 1 to 5cm). The mean bother score on genital prolapse in these 14 patients dropped significantly from 50 before to 7 after surgery (p 0.01).

In seven patients (18%) postoperatively the posterior compartment was classified as stage II. Postoperative points Bp were all -1 and had improved from 1 to 4 cm. In our opinion it is debatable whether one should classify patients with a stage II prolapse (that is leading edge is >-1<+1) without prolapse symptoms as surgical failure. In addition one has to realize that in the normal population ICS stage II

prolapse is commonly seen. Swift et al. reported 48 % and found that prolapse complaints increased significantly when the leading edge of the prolapse reached beyond the hymenal remnants, which finding led to their statement that this helps defining *symptomatic* pelvic organ prolapse.[25]

The functional results of the operations, in terms of diminished bother scores in the various domains were good. With the exception of incontinence on the UDI and pain on the DDI all bother scores on UDI and DDI decreased significantly. It should be emphasized that urinary incontinence was not the indication for surgery in these patients. In another Dutch study of sacrospinous hysteropexy with classical anterior repair the same questionnaire was used but unfortunately only postoperatively.[26] Postoperative bother scores on the domains of overactive bladder and obstructive micturition in our study are higher than in that study, but the technique used in that study (hysteropexy) was essentially different from ours (no apex fixations). Since pre--operative values of the two mentioned domains are missing in that study an actual comparison is not possible. The scores on the domain of genital prolapse in our study decreased sharply, which reflects the high efficacy of repair surgery on the symptoms of vaginal prolapse.

Erosion and shrinkage

Erosions and potential 'shrinkage' induced by synthetic mesh might cause deformation of the vagina. Shrinkage is provoked by chronic inflammatory reactions to the mesh.[27] These reactions may lead to fibrosis, with scarring and retraction of the surrounding tissues, which subsequently 'compresses' the underlying mesh. The lack of any clinically detectable shrinkage in our patient group was comparable with findings in the quoted animal study.[15] However, this issue requires further attention during longer-term follow-up.

In the retrospective series evaluated by the 2 other mentioned research groups, Dwyer et al. observed erosions after a mean follow-up of 29 months (range 6-52) in 9% of patients. They considered that the risk of erosion was not only related to the type of graft material, but also to the experience of the surgeon.[12] Milani et al. reported an overall erosion rate of 10% after a median follow-up of 17 months (range 3-48) and a high rate of postoperative dyspareunia. Therefore, they put forward arguments to abandon the use of synthetic mesh in vaginal prolapse surgery.[13] The erosion percentage of 5,6% in our study is low compared to other studies with non--coated heavier polypropylene mesh. The median follow-up in our study however was relatively short. We could not confirm the high rate of postoperative dyspareunia as found by the research group of Milani et al.[13] We found no statistically significant differences in the answers given to the questions as shown in table 4 before and after surgery. All 4 cases of erosion were detected in the posterior compartment, in the vaginal scar. None were seen in the apex of the vagina or posterior commisura, or in the anterior compartment. In these vaginal wall repairs, the mesh was placed beneath the vaginal epithelium so that it covered the plicated fascial layers of the bladder and rectum, respectively. It is a matter of debate as well whether positioning the mesh under the fascial layer of the rectum could have decreased the risk of erosion, as

was questioned by one of the other research groups.[13] After using collagen coated low-weight polypropylene mesh in tension-free vaginal repair surgery, De Tayrac et al. reported erosion rates of 6% on the anterior wall and 1,3% on the posterior wall.[24] These lower percentages provide further evidence of the advantages of using low-weight mesh and/or coating to reduce erosion rates.

Despite the prospective nature and the use of validated questionnaires and standardized POPQ, a limitation of our study is the relatively short follow-up period. Continued prospective follow-up will show whether the mesh related morbidity stays at the level of the presented data. To answer the question of the anatomical efficacy of augmentation of conventional colporrhaphy with Ti-mesh®, a well--powered randomized controlled study, comparing Ti-mesh versus non-mesh surgery, is necessary. We did not detect any erosion in the anterior vaginal compartment, but the risk of prolapse recurrence seems highest in that anatomical region.[4] Therefore, to our opinion, future research should mainly focus on this compartment and we strongly agree with the conclusion drawn in a recent evidence-based review on the surgical management of anterior vaginal wall prolapse that particularly controlled studies are necessary.[28]

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4

TROCAR-GUIDED TOTAL TENSION-FREE VAGINAL MESH REPAIR OF POST-HYSTERECTOMY VAGINAL PROLAPSE

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ABSTRACT

Introduction and hypothesis

The objective of this study was to report on one-year anatomical and functional outcomes of trocar-guided total Tension free Vaginal Mesh (Prolift™) repair for post hysterectomy vaginal vault prolapse with one continuous piece of polypropylene mesh.

Methods

We conducted a prospective observational cohort study on 46 patients. A minimum sample size of 35 patients was needed to detect a recurrence rate of less than 20% at 12 months. Instruments of measurement: POP-Q and validated questionnaires.

Results

Overall anatomical success was 91% (95% CI 83-99), with significant improvements in experienced bother- and quality of life. Mesh exposure occurred in seven patients (15%). Adverse effects on sexual functioning could not be detected.

Conclusion

Trocar-guided total Tension free Vaginal Mesh (Prolift™) repair with one continuous mesh for post hysterectomy vaginal vault prolapse is well tolerated and anatomically and functionally highly effective. Results of controlled trials will determine its position in the operative armamentarium.

INTRODUCTION

Pelvic organ prolapse in women is common, affecting 50% of parous women over 50 years of age, with a lifetime prevalence risk of 30-50%.[1] A challenging aspect of pelvic organ prolapse is the treatment of the prolapsed vaginal vault. The incidence of post hysterectomy vaginal wall prolapse that requires surgery has been estimated at 1.3 per 1000 women-years.

The risk of prolapse surgery was 4.7 times higher in women whose initial hysterectomy was indicated by prolapse and 8.0 times higher if preoperative prolapse stage II or more was present.[2]

The surgical treatment of vaginal vault prolapse can either be performed by vaginal or abdominal route. A prospective randomized clinical trial on vault prolapse, which compared the abdominal sacral colpopexy with the vaginal sacrospinous colpopexy, showed similar results in both groups with regards to subjective and objective postoperative anatomical assessment and impact on quality of life, but found that the abdominal route was associated with a longer operating time, slower return to activities of daily living, and greater cost than the vaginal sacrospinous colpopexy.[3] Both techniques have some drawbacks. Prolapse of the anterior compartment following sacrospinous colpopexy and of the posterior compartment following abdominal sacral colpopexy are well reported.[4, 5] Vice versa, treatment of the anterior and / or posterior compartment alone will invariably affect the vaginal vault.[6] The ideal solution therefore would be a surgical approach with minimal morbidity that simultaneously treats all three compartments equally successful.

A number of synthetic implant materials with surgical instrument kits is currently commercially available. The rationale for using these are to decrease surgical failures. One of these surgical kits is designed for the total vaginal repair of vault prolapse with one continuous mesh interposition on the anterior, middle and posterior compartment and aims to be a bilateral sacrospinous ligament suspension as well (Prolift™, Ethicon, Somerville, NJ, USA). The first data on the efficacy and safety of this novel trans vaginal mesh technique are reported from retrospective case series and do not explicitly focus on this total vaginal mesh treatment with one continuous mesh for vault prolapse.[7, 8] Prospective data on this tension free vaginal mesh technique were scarce and with short term follow-up.[9] Only one paper on trocar-guided vaginal mesh repair shows a prospective follow-up of one year, but the authors do not discriminate between the combined anterior and posterior repair with preservation of the uterus and a true total repair with one continuous mesh for vaginal vault prolapse.[10]

The aim of this paper is to exclusively report on the efficacy and safety of the total Tension free Vaginal Mesh (Prolift™) repair with one continuous piece of mesh for the anterior, middle and posterior compartment in case of post hysterectomy vaginal wall prolapse.

MATERIAL AND METHODS

In September 2005 an ongoing prospective observational cohort study with the Prolift™ pelvic floor repair system was started in two urogynecological centres in

the Netherlands, the Reinier de Graaf Hospital in Delft and the Radboud University Nijmegen Medical Centre.

After obtaining informed consent consecutive patients with recurrent vaginal wall prolapse stage II or more or with a primary vaginal wall prolapse stage III or more were enrolled in this study. At the beginning of 2009 297 patients were included. One hundred ninety-six patients (66%) had completed their one-year follow-up. Of those 46 patients (24%) underwent the total continuous vaginal mesh procedure for vault prolapse. Four surgeons who were trained prior to the start of the study performed surgical procedures. Most postmenopausal patients were treated with topical estrogen 6-8 weeks prior to surgery and continued this treatment postoperatively when considered necessary. Concomitant anti-incontinence surgery was not performed in this patient series, in order to prevent increased risk on complications as reported earlier by us.[11] All patients were counselled about this strategy prior to surgery.

Preoperatively genital prolapse was quantified in the dorsal lithotomy position using the POP-Q measurement system.[12] Postoperatively POP-Q measurements were performed at both 6 and 12 months.

Surgical procedure

Peroperative antibiotic prophylaxis was given with a single shot of Cefalozine-Natrium (Kefzol® Lilly, the Netherlands) and Metronidazol (Flagyl® Aventis Pharma BV Hoevelaken, the Netherlands). Patients were positioned in the dorsal lithotomy position with their hips flexed to about 110°. The anus was covered with Tegaderm®. After liberal use of hydrodissection (Lidocaine hydrochloride monohydrate 200mg with epinephrine hydrogen tartrate100µ g in 20 ml - Astra Zeneca BV Zoetermeer the Netherlands- diluted in 100 ml of 0.9% saline solution) an anterior midline incision was made which included full thickness of the fibromuscular wall of the vagina from about 2.5 cm distal from the external urethral meatus to about 2 cm distal of the vaginal apex. Bilateral mostly blunt and incidentally sharp dissection was used to open the vesicovaginal fascia on each side in order to reach distally the cranial side of the ischial spine, the arcus tendineus fascia pelvis and the retropubic space. The transobturator insertion of the cannula equipped guides and retrieval devices has extensively been described elsewhere and was not altered in our hands.[7] Then, after hydrodissection of the posterior vaginal wall, a full thickness vaginal wall incision was made to the vaginal apex leaving an apical bridge of vaginal tissue of about 3cm to the anterior incision. The pararectal space was bilaterally bluntly dissected until the caudal side of the ischial spines were reached and the sacrospinous ligaments were properly identified. The cannula equipped guides were used to perforate and pass the sacrospinous ligaments about two cm medial from the ischial spines as described in the paper by Fatton et al.[7] Then a canal was carefully dissected under the apical bridge of the vaginal vault in order to allow passage of the posterior part of the total Prolift™ mesh. After gloves were changed to minimize colonisation of bacteria and decrease infection risk, a slender forceps was used to gently pull the posterior part of the mesh through the previously dissected canal at the level of the vault in such a manner that the middle part of the mesh exactly fitted under this bridge of vaginal tissue (figure 1). After fixation of the

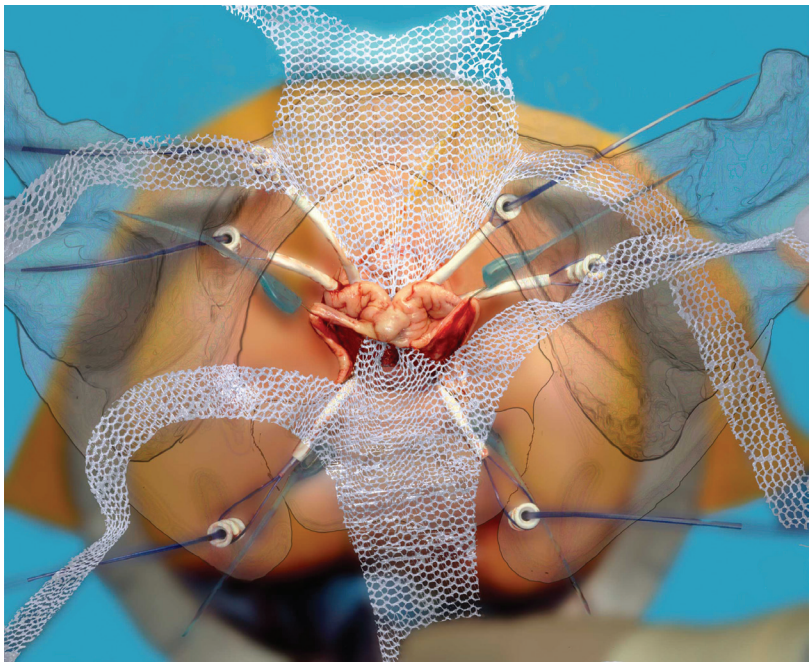

Figure 1. Total mesh in position under the vaginal apical bridge (Medical photography: Mr. Ruud van de Voorde, Image manipulation Mr. George Bazan).

mesh with two Vicryl 00 sutures at the level of the bladder neck and two Vicryl 00 sutures close to the posterior vaginal commisura the four anterior and two posterior mesh arms were gently pulled through the cannulas by the respective retrieval devices. The mesh was carefully spread out to avoid unnecessary mesh folding after which the full thickness of the anterior and posterior vaginal walls were closed with a running Vicryl 00, without any prior vaginal wall dissection. After repositioning the vagina with two Breisky specula to its physiological anatomical position the cannulas were gently withdrawn and finally a finger in the rectum gently uplifted the posterior mesh with the intention to prevent future tension on the rectum, after possible shrinkage of the mesh. The cutaneous remnants of the mesh arms were cut and the small skin incisions closed with rapidly dissolving Vicryl 000. An iodized gauze pack was left in the vagina for at least 24 hours. The indwelling catheter was removed on the second postoperative day.

Study endpoints

We defined the primary endpoint of this study to be prolapse recurrence at 12 months. Anatomical failure was defined if at least one of the compartments at 12 months was classified as POP ≥ stage II. Anatomical success was defined as overall POP stage 0 or I.

Secondary endpoints were anatomic success per compartment, per- and postoperative morbidity, and change in experienced bother, quality of life and global impression of change at 6 and 12 months, as well as effects on sexual functioning.

Sample size

We defined study success as an upper 95% Confidence Interval for recurrence <20% at 12 months. We assumed that an estimated success of 90% at 12 months in the mesh treated compartments would be realistic.[8] With this estimated 90% success rate, a two-sided 95% Confidence Interval of 10% was allowed, which meant that we needed a minimum sample size of 35 patients for this study.

Data collection

To obtain data on the functional efficacy and impact on patients quality of life the standard urogynecological questionnaire of the Dutch Pelvic Floor Society was used at baseline and at 6 and 12 months postoperatively. This questionnaire contains the validated Dutch versions of the Pelvic floor Distress Inventory (UDI and DDI), the Pelvic Floor Impact questionnaire (IIQ), Patients Global Impression of Improvement (PGI-I) and questions on sexual functioning.[13, 14] All data were entered into a SPSS 16.0 database. Baseline and surgical data are presented as median (range), complications as numbers with corresponding percentages. Differences in numbers were tested using Pearson's Chi-square test. Mean domain scores and standard deviations were calculated on the domains of UDI, DDI and IIQ. Differences in means between baseline and postoperative scores at 6 and 12 months were tested with the paired-samples t- test. A p-value ≤ 0.05 was considered significant.

RESULTS

Forty-six consecutive patients who were operated according the total vaginal mesh procedure (Prolift™) for post hysterectomy vaginal wall prolapse were analysed. For various reasons we missed 7 patients at the 6 months visit. At the 12 months visit one patient refused to come for POP-Q examination, since she stated to have no complaints. We could not convince her of the usefulness of this check-up. She was willing though to send us her completed questionnaire. One other patient was not able to complete her 12 months questionnaire because of progressive cerebral dementia, but she was willing to be examined for POP-Q measurements. Median age was 66 (38-86) years. All but one patient (98%) had undergone previous prolapse surgery, of whom 4 (9%) more than once. Baseline and other surgical characteristics are presented in table 1.

Anatomical results

Baseline, 6 and 12-month data per POP-Q variable, overall POP stage and POP stage per compartment are shown in table 2. At baseline 40 patients (87%) were classified having a vaginal prolapse with the leading edge at POP stage III or IV and 6 (13%) at stage II.

Table 1. Baseline, surgical characteristics & complications.

Baseline characteristics (N: 46)	
Age (years)	66 (38-86)
BMI (kg/m^2)	25 (21-32)
Parity (n)	2 (0-5)
Postmenopausal	43 (93%)
Abdominal hysterectomy	13 (28%)
Prior prolapse related surgery	45 (98%)
Vaginal hysterectomy	33 (72%)
Anterior repair	25 (54%)
Posterior repair	21 (46%)
More than one prolapse repair	4 (9%)
Prior surgery for incontinence	3 (7%)
Surgical characteristics	
Duration of surgery (minutes)	80 (54-109)
Bloodloss (ml)	100 (50-1300)
Spinal analgesia	21 (46%)
General anesthesia	25 (54%)
Duration of stay indwelling catheter (days)	2 (1-6)
Hospital stay (days)	4 (3-8)
Complications	
> 500ml Bloodloss	2 (4%)
Bladder lesion	0
Rectal lesion	0
Postoperative hematoma	2 (4%)
Urinary retention after removal catheter	8 (17%)
Accumulated mesh exposure (12 months)	7 (15%)
Exposure in anterior compartment	3
Apical exposure	2
Exposure in posterior compartment	2

Data are presented as median (range) or number (percentage).

Twelve months after surgery 41 out of 45 patients (91%: 95% CI 83-99) fulfilled the criteria of an overall anatomical successful repair. Four (9%) were thus classified as anatomical failures. One of these was classified as stage III (C+4). She later underwent an abdominal sacrocolpopexy. Mean changes from baseline per POP-Q variable at 6 and 12 months are shown in table 2 as well. All changes are considerable and significant. The size of the genital hiatus decreased significantly with more than 1 cm, although surgery on the vaginal introitus was performed in none. The mean total vaginal length decreased statistically significant with 0.3 cm, but seemed not to be clinically significant.

Table 2. Anatomical data per POP-Q variable and POP stage at baseline, 6 and 12 months

POP-Q variable		Baseline (N: 46)	6 months (N: 39)	Change from baseline	12 months (N: 45)	Change from baseline
Ba		3.0 (2.6)	-2.7 (0.5)	5.3 (2.2)*	-2.5 (1.1)	5.4 (2.4)*
C		-0.2 (4.7)	-7.4 (1.5)	6.5 (4.2)*	-7.1 (2.3)	6.7 (4.6)*
Bp		1.9 (2.9)	-2.6 (0.7)	3.9 (2.3)*	-2.4 (1.2)	4.2 (2.6)*
TVL		8.8 (1.2)	8.5 (1.1)	0.2 (1.2)	8.5 (1.2)	0.3 (0.9)†
GH		4.8 (1.3)	3.5 (1.0)	1.3 (1.3)*	3.5 (1.0)	1.2 (1.4)*
PB		3.5 (1.2)	3.5 (0.9)	0.0 (1.0)	3.5 (0.9)	0.0 (1.0)
POP Stage		**Baseline**	**Success at 6 months**		**Success at 12 months**	
Anterior	0	-	26 (66.7%)	100%	31 (68.9%)	95.6%
	I	2 (4.3%)	13 (33.3%)		12 (26.7)	
	II	12 (26.1%)	-		1 (2.2%)	
	III	30 (65.2%)	-		1 (2.2%)	
	IV	2 (4.4%)	-		-	
Apical	0	1 (2.2%)	33 (84.6%)	97.4%	36 (80%)	95.6%
	I	25 (54.3%)	5 (12.8%)		7 (15.6%)	
	II	3 (6.5%)	1 (2.6%)		1 (2.2%)	
	III	14 (30.4%)	-		1 (2.2%)	
	IV	3 (6.6%)	-		-	
Posterior	0	1 (2.2%)	26 (66.7%)	94.9%	30 (66.7%)	91.1%
	I	3 (6.5%)	11 (28.2%)		11 (24.4%)	
	II	20 (43.5%)	2 (5.1%)		3 (6.7%)	
	III	20 (43.5%)	-		1 (2.2%)	
	IV	2 (4.3%)	-		-	
Overall	0	-	15 (38.5%)	94.9%	15 (33.3%)	**91.1% (82.8-99.4)‡**
	I	-	22 (56.4%)		26 (57.8%)	
	II	6 (13%)	2 (5.1%)		3 (6.7%)	
	III	37 (80.5%)	-		1 (2.2%)	
	IV	3 (6.5%)	-		-	

Data are presented as mean (± standard deviation) for POP-Q variable and as number (percentage) for POPstage. Ba: most descendant point at anterior vaginal wall, C: vaginal apex, Bp: most descendant point at posterior vaginal wall (all in cm distance from the hymenal remnants). TVL: Total Vaginal Length, GH: Genital Hiatus, PB: Perineal Body length in cm (± standard deviation). * P level <0.001 (paired samples t-test), † P level 0.018 (paired samples t-test), ‡ 95% confidence interval.

Morbidity

In table 1 is shown that there were no bladder- or rectal perforations in this patient series. In two patients a hematoma presented postoperatively in the buttock region, which resolved spontaneously within 10 days. A total number of seven patients (15%) were found to have a small mesh exposure; four at the 6 months follow-up and another three at the 12 months visit. Three of these mesh exposures were located on the anterior scar, two close to the level of the vault, and two in the posterior scar. All of these were asymptomatic and measured between 5 and 20 mm in size. All seven

patients were initially treated with topical estrogens and for reasons of insufficient healing the tiny mesh exposure was excised in five patients in a day-care procedure. The two other patients preferred an expectant management.

Functional results

In table 3 data on sexual functioning at baseline and 12 months are shown.

The percentages of patients reporting dyspareunia before and after operation were equal (37%). De novo dyspareunia occurred in two patients (18%). In another two (28%) however dyspareunia disappeared after surgery.

Table 3. Data on sexual function at baseline and 12 months

	Baseline			12 months			P*
Regular intercourse	19 of 42 (45%)			19 of 43 (44%)			N.S
Dyspareunia	7 of 19 (37%)	A little Rather much Very much	2 3 2	7 of 19 (37%)	A little Rather much Very much	2 2 3	N.S
De novo dyspareunia				2 of 11 (18%)	A little Rather much	1 1	
Resolved dyspareunia				2 of 7 (28%)			
De novo intercourse				3 of 23 (13%)			
Abstained intercourse				4 of 19 (21%)			

Data presented as number of patients (percentages). *Pearson Chi-square test.

Table 4 shows functional data in the domains of UDI, DDI and IIQ as well as PGI-I.[13, 14] Scores ranged between 0 (least bother and best quality of life) to 100 (maximum bother and worst quality of life). Six and 12 months after surgery 94 and 93% of patients respectively stated to be much to very much better compared to their baseline situation.

DISCUSSION

To our knowledge this study is the first of considerable size that prospectively and specifically evaluates the efficacy and safety of the Total Tension free Vaginal Mesh repair with one continuous piece of polypropylene mesh for all three compartments of the prolapsed vaginal vault. The Prolift™ total prolapse repair system is unique in this respect and at present the only available kit that offers the possibility of such a complete repair. It aims at support of the weakened vaginal walls of the anterior and posterior compartments and at suspension of the middle compartment by means of a bilateral sacrospinous ligament fixation and thus restoring Delancey level I support.[15] Other mesh kits are designed to treat the anterior and posterior compartments, either alone or simultaneously, with a separate (split) mesh. Suspension of the vault in these procedures is not achieved by a bilateral sacrospinous ligament fixation, but by means of bilateral infracoccygeal sacropexy as described by Petros.[16] Most data on these

Table 4. Functional data on domains of UDI, DDI, and IIQ at baseline, 6 and 12 months & PGI-I

	Baseline	6 months (N: 39)	P *	12 months (N: 45)	P **
Domains *UDI*					
Prolapse	69.1 (33.6)	0.4 (2.7)	<0.001	2.3 (11.3)	<0.001
Incontinence	24.2 (29.5)	16.2 (18.5)	0.250	14.2 (17.1)	0.122
Overactive bladder	31.6 (30.6)	10.5 (17.6)	0.002	11.1 (18.3)	0.001
Obstructive micturition	29.4 (29.9)	7.4 (17.6)	0.002	5.4 (11.3)	<0.001
Pain	26.7 (28.4)	12.6 (20.6)	0.005	10.2 (17.7)	0.001
Domains *DDI*					
Constipation	8.3 (14.6)	3.8 (9.1)	0.205	2.4 (6.9)	0.291
Obstructed defaecation	12.1 (17.2)	4.3 (8.9)	0.009	3.5 (7.7)	0.003
Pain	7.7 (19.0)	4.2 (12.8)	0.366	2.4 (10.8)	0.146
Incontinence	7.3 (13.5)	3.2 (7.8)	0.090	2.1 (6.7)	0.103
Domains *IIQ*					
Physical functioning	32.5 (34.0)	8.1 (2.1)	0.002	9.3 (23.3)	0.001
Mobility	34.5 (25.8)	9.1 (12.7)	0.062	11.9 (20.2)	<0.001
Emotional Health	23.1 (27.9)	5.2 (8.9)	0.002	9.9 (18.7)	0.001
Social Functioning	18.1 (18.9)	3.5 (7.8)	0.002	6.9 (13.7)	<0.001
Embarrassment	16.7 (23.6)	2.8 (6.3)	0.016	7.8 (16.5)	0.062
Patients Global Improvement *(PGI-I)*		**at 6 months**		**at 12 months**	
Very much better		50%		48%	
Much better		44%		45%	
Little better		6%		5%	
No change		-		-	
Little worse		-		2%	

UDI: Urinary Distress Inventory, DDI: Defaecatory Distress Inventory, IIQ: Incontinence Impact Questionnaire. Scores range between 0 (least bother and best quality of life) to 100 (maximum bother and worst quality of life).
Values presented as means ± standard deviation. * P value between baseline and 6 months (paired samples t-test). ** P value between baseline and 12 months (paired samples t-test).
PGI-I: Patients Global Impression of Improvement (percentage of patients with answer).

procedures are derived from congress abstracts, retrospective reports or studies with short follow-up.[7, 9, 17] Only few data are published with a medium long term follow--up, but none of these focuses exclusively on the total repair with one continuous piece of mesh.[8, 10]

Anatomical effect

Considering the high percentage of patients with recurrent prolapse (98%) and high stage POP (III and IV) in this study group at baseline (87%) and the follow-up period of one year, the overall anatomical success of 91% is respectable. This is also reflected in the mean changes of the three most relevant POP-Q variables (Ba, C, Bp) between baseline and 12 months, which even exceed those reported by other authors.[8] Anatomical success rates per compartment, are comparable with that report.

Anatomical results in this study seem somewhat better than those reported by the Scandinavian group, who reported 79-82% for the anterior compartment and 81-86% for the posterior compartment.[10] Neither of these authors however makes a distinction between the combined anterior and posterior mesh treatment and the total treatment with one continuous piece of mesh. A clear comparison is therefore not possible. The Scandinavian group reported the combined results of 26 participating centres, while we report on only two major centres. Therefore the number of procedures performed per surgeon and possibly the experience related to this might be different. Only one small other study reported on 21 Prolift™ total repairs with one continuous piece of mesh and showed an anatomical success of 87% at 12 months.[18] The fairly small number of patients that could be evaluated in that study makes 95% Confidence Intervals rather wide (14%) and results less comparable.

The success rate of 95% for restoration of level I support of the apex is comparable with the 74-100% success rate of apical support in abdominal sacrocolpopexy and the 89-97% success rate for restoration of apical support by sacrospinous ligament fixation.[19-21] The advantage of this total vaginal mesh procedure however is that it adds support to both other vaginal compartments as well, and compared to the abdominal sacrocolpopexy, has a shorter operation time and can be considered as a relatively minimally invasive treatment.

At 12 months the measured total vaginal length was a mean 0.3 cm shorter than at baseline. This slight shortening probably is due to some shrinkage of the mesh, which actually is not a shrinkage of the material itself, but rather a retraction due to fibrotic reactions to the polypropylene mesh.[22] Although this slight shortening is statistically significant we, as other authors, could not detect any clinical significance of this finding.[10] If shrinkage continues however, this could become relevant in the future, so longer follow-up is mandatory.

Surgical and peri-operative morbidity

In this series of patients with a total Prolift™ repair we experienced no bladder or rectal injuries, which in the large retrospective French series are well reported in percentages of 0.7 and 0.15 respectively.[23] The rate of postoperative hematomas in our series is comparable with those of the Scandinavian and French reports.[10, 23]

Mesh exposure

One important adverse effect of mesh surgery is the fairly high number of mesh exposures. We found seven (15%) after 12 months. Interestingly we found none at the first postoperative visit at six weeks, but four at 6 months and another three at the 12-month visit. Neither of these patients was symptomatic. Therefore a very careful follow-up even beyond 12 months seems mandatory. The number of exposures in the remaining 150 patients of our database who completed their 12 month follow--up (at present data are being processed for submission) is 10% and not statistically significant different from the percentage in this series (Pearson's Chi-square 1.067; p 0.301). The Scandinavian group reported similar findings; the erosion percentage rose

from 7% at two months to 11% at twelve months.[10] A similar percentage (11.3%) is also reported in the large retrospective French series.[23] Since we are not aware of the natural development of these most asymptomatic mesh erosions, we felt the urge to treat them. Initially with topical estrogens, but as this was not sufficient in most of them, we performed a minor mesh excision in five (11%) patients. The remaining two patients who preferred an expectant management are still without symptoms.

Of these seven patients with a tiny mesh exposure, four didn't have intercourse at baseline, but one of these had resumed intercourse at 6 months. One other patient continued to have intercourse. Neither of both complained of dyspareunia. Of three patients in whom a mesh exposure was detected at the 12-month visit, two had intercourse at baseline. At 12 months one of these continued to have intercourse without symptomatic dyspareunia and the other patient had abstained from intercourse for other reasons than pain. Apparently sexual intercourse by these patients was not hindered by the presence of these minor mesh exposures.

We found that the mean duration of surgery in the group of patients who developed a mesh exposure (92 ± 13) was 14 minutes longer than in those who did not (78 ± 15). Whether this is a significant item in this relatively small group of patients remains unclear. This study group however represents a fairly complex group of patients with recurrent prolapse in all but one. The special technique, which leaves a small bridge of vaginal vault intact, might jeopardize the vascularisation of the vaginal tissue and could be responsible for poor wound healing and thus mesh exposure. In our opinion though the rate of mesh exposures is still too high and determinants other than those already published need to be discovered to lower this incidence.[23-25]

Functional effects

Some earlier studies warned for the use of synthetic mesh in prolapse surgery because of high risk of dyspareunia.[26] Other authors, who used modern kits with low weight polypropylene designed by other companies, such as coated polypropylene (Ugytex, Sofradim, France) or the Perigee Transobturator Prolapse Repair System (American Medical Systems, Minnetonka, MN) reported de novo dyspareunia after one year in 13% and 9% of patients respectively.[27, 28] We detected de novo dyspareunia in two out of eleven patients (18%), but these are small numbers. On the other hand the percentages of patients having intercourse or dyspareunia at baseline and 12 months were practically identical. In two out of seven patients (28%) who suffered from dyspareunia at baseline this complaint was no longer present at 12 months. Furthermore three out of twenty three patients (13%) who were not having intercourse at baseline had resumed this at 12 months. These data show that prolapse itself is a cause of dyspareunia and prolapse repair, in this case with a fairly large synthetic mesh, is able to resolve this problem in some. These results are comparable with observations done by the Scandinavian group, who used the short form of the PISQ questionnaire.[29] They observed an overall deterioration of sexual function scores in women one year after trocar-guided transvaginal mesh surgery. However, the worsening was attributed to decreased scores on behavioural-emotive

and partner-related items, such as partner inability to have an erection. Dyspareunia neither improved, nor worsened, as is our observation.[30] Although the rate of de novo dyspareunia seems low with the present light weight meshes we should remain cautious and await longer-term follow-up for realistic interpretations.

From a patients point of view probably more important than the objective anatomical success is the subjective improvement in experienced bother and quality of life. This is clearly shown by the stable percentage of patients (93%) that experienced their situation to be much to very much better 12 months after surgery compared to baseline.

The improvements in the various domains of UDI, DDI and IIQ remain stable between 6 and 12 months and are highly significant compared to baseline, except for the domains of incontinence of the UDI and constipation, pain and incontinence of the DDI and embarrassment of the IIQ. As mentioned before, so far it has been our strategy not to treat patients simultaneously for their prolapse and potentially manifest or masked stress urinary incontinence. All patients were counselled about this strategy before surgery. Only one patient needed and underwent a midurethral sling procedure between her 6 and 12 months visit because of unmasked stress urinary incontinence.

In our opinion the strengths of this study are its prospective nature and the use of internationally accepted instruments of measurement such as validated questionnaires and POP-Q, the follow-up period of one year, as well as the high follow-up rate and data acquisition in all patients. A limitation of this study on the other hand is that not all POP-Q measurements were performed by an independent examiner.

Conclusion

The trocar-guided total tension free vaginal mesh repair for post hysterectomy vaginal vault prolapse with one continuous piece of polypropylene mesh is very well tolerated and anatomically and functionally highly effective at 6 and 12 months follow-up. Whether this procedure is more effective and safe than other forms of prolapse surgery remains to be determined in randomized controlled trials.

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5

TROCAR-GUIDED MESH REPAIR OF VAGINAL PROLAPSE USING PARTIALLY ABSORBABLE MESH: 1-YEAR OUTCOMES

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ABSTRACT

Objective

To evaluate anatomical and functional outcomes at 1-year following trocar-guided transvaginalprolapse repair using a partially absorbable mesh.

Study design

Prospective multi-centre cohort study at 11 international sites.One hundred twenty--seven patients with pelvic organ prolapse stage ≥ III were operated and evaluated at 3 months and 1year post-surgery compared to baseline. Instruments of measurements: POP-Q, PFDI-20, PFIQ-7, PISQ-12and PGI-C.

Results

Anatomic success, defined as prolapse stage ≤ I in the treated vaginal compartments, was 77.4% (95% CI 69.0%-84.4%). Significant improvements in bother, quality of life and sexual function were detected at 3 months and 1 year compared to baseline. At one year following surgery, 86.2% of patients indicated their prolapse situation to be 'much better'.
Mesh exposure rate was 10.2% and rate of de novo dyspareunia 2% at 1 year.

Conclusion

These results demonstrate improved anatomic support, associated with excellent functional improvements, without apparent safety concerns.

INTRODUCTION

Pelvicorganprolapse (POP) is a common problem and may occur in up to 50% of parous women.[1] A Dutch cross-sectional study demonstrated a prevalence of symptomatic POP as high as 11,4%.[2] In 2003 over 300,000 women underwent prolapse surgery in the United States, indicating that POP is among common indications for surgery.[3]

There is increasing evidence that the tension-free vaginal insertion of prosthetic mesh in patients with symptomatic POP reduces the chance of anatomic failure.[4-8] The introduction of these new materials in pelvic reconstructive surgery has introduced new kinds of morbidity. Among the most prevalent complications are mesh exposure and shrinkage of tissue around the mesh. These may result in pelvic pain and dyspareunia.[9, 10] De novo dyspareunia following traditional POP repair ranges between 14.5-36.1% and a recent retrospective study reported a similar rate (16.7%) following repair with a mesh kit system.[1, 11, 12] Prospective studies and a large retrospective study using such mesh, have reported mesh exposure rates that ranged between 10 and 15%.[13-16]

The superiority of the light-weight large pore mesh compared to conventional heavier-weight mesh with regard to reduced numbers of long-term complications and increased comfort, has been clearly demonstrated in a review on inguinal hernia repair.[17] A trocar-guided mesh system with a non-absorbable, mono-filament polyprolyene mesh was introduced in 2005.[12, 14-16, 18-20] One of the key rationales for adopting a new, lighter-weight mesh with improved directional elastic properties was to minimize tissue shrinkage, which may lead to dyspareunia. This new mesh is composed of a fifty-fifty blend of monofilament non-absorbable polypropylene and absorbablepolyglecaprone 25.[21, 22] Before absorption, this mesh weighs 57 g/m^2. Full absorption after 90-120 days results in a final weight of 31 g/m^2, as opposed to the 45 g/m^2 of the original polypropylene mesh. Due to warp knitting, this mesh provides increased elasticity in the longitudinal direction and has larger pores compared to the original mesh to allow more tissue in-growth.

The primary objective of this study was to assess anatomic and functional outcomes with this new mesh one year post-surgery. The secondary objective was to assess adverse events, particularly pain and dyspareunia.

MATERIALS AND METHODS

The study protocol and informed consent documentation received ethics committee / institutional review board approval at all participating sites. The trial was registered at ClinicalTrials.gov; NCT00833001. Eleven urogynecological centres from Belgium, France, Germany, the Netherlands and the US enrolled patients between April and October 2008; one year follow-up visits were completed by November 2009. All patients gave written informed consent prior to participation in the study. Inclusion criteria were POP stage III or IV, according to the Pelvic Organ Prolapse Quantification (POP-Q) classification system.[23] Concurrent hysterectomies and / or perineal repairs were allowed, but exclusion criteria were: other additional surgical repair of prolapse,

including paravaginal repair, sacrocolpopexy and colporrhaphy in a non-mesh treated compartment; previous prolapse repair using mesh; systemic diseases known to affect bladder or bowel function and any medical or psychiatric condition that could potentially affect the patient's ability to complete study visits.

All patients underwent the standardized trans-vaginal mesh placement technique (GYNECARE PROLIFT+M Pelvic Floor Repair System, ETHICON, Somerville, NJ; referred to as Prolift+M). All surgeons were experienced with the procedure prior to participation.[18] Depending on the site of prolapse, the mesh repair could be anterior, posterior or total; in patients with an intact uterus, the total mesh was cut. Concurrent hysterectomies, perineal repairs and/or mid urethral sling procedures were performed at each surgeon's discretion. Cystoscopy was required for repairs involving the anterior compartment. All procedures were performed under antibiotic coverage, according to the standard of each participating site.

Pelvic examination, including the POP-Quantification system was performed at baseline, 3 months and 1 year post-surgery.[23] Subsequent follow-up evaluations will be obtained at 2 and 3 years post-surgery.

The primary outcome was defined as anatomic success in the treated compartment at one year, being a POP-Q Stage ≤ I, without further surgical re-intervention for POP in that compartment. A priori, an alternate outcome measure was defined: leading edge of prolapse proximal to the hymen (i.e. <0 cm) in the treated compartment at one year, without further re-operation. To address the untreated compartment, a secondary outcome was the incidence of *de novo*prolapse, defined as occurrence of post-operative prolapse (ICS Stage ≥ II) in the untreated compartment, provided there was no pre-operative defect in that compartment (i.e. ICS Stage ≤ 1).

Other secondary outcomes were self-completed patient-reported outcome (PRO) measures, administered at 3 months and 1 year. POP-specific symptom bother and quality of life (QoL) were measured by the short form versions of the Pelvic Floor Distress Inventory (PFDI-20) and Pelvic Floor Impact Questionnaire (PFIQ-7), respectively.[24] The validated American English versions of these questionnaires were used at US sites. For use in German, Dutch, Flemish and French languages, the American version underwent translation and cultural adaptation in accordance with the International Society of Pharmacoeconomics and Outcomes (ISPOR) guidance.[25] To gauge patients' subjective impression of improvement specific to the POP-intervention, the Patients Global Impression of Change (PGI-C), was used.[26]

An internationally recognised measure of general health status, EQ-5D, was used thatenables comparisons of impact across different diseases.[27]

For sexually active women, the short-form of Pelvic Organ Prolapse/Urinary Incontinence Sexual Function (PISQ-12) questionnaire was administered to evaluate sexual function at baseline, 3 months and 1 year.[28] The validated English version was used at the English speaking sites, while the other language versions underwent the same translation and cross-cultural adaptation as described above. Dyspareunia was assessed at baseline, 3 months and 1 year in sexually active patients by asking "If the subject has been sexually active in the last 6 months / since the study surgery, have they experienced dyspareunia?"

Pelvic pain was evaluated during routine life and/or during pelvic examination at baseline and follow-up visits. The incidence of mesh contraction and vaginal wall stiffness was determined if pain was elicited on gentle palpation of mesh and its attachment points during pelvic examination. A pre-determined safety outcome was the incidence of any exposures / erosions including location.

Sample size estimation:assuming that anatomic results of this new mesh were similar to the original polypropylene mesh, an anatomic success rate in the treated compartment of 80% stage ≤ I was realistic. With a two-sided 95% confidence interval of 7% at least 125 subjects were needed to be enrolled. Anticipating on a drop out rate over the first year of 5%, this would ensure 118 subjects to be evaluable at 1 year.

Results are summarized as follows; mean, standard deviation, minimum, median, maximum and 95% CI for continuous data and number, percent for discrete data. Student t-test was used to calculate p-values where appropriate for change from baseline to 3 months and 1 year. The 95% CI for success rates were constructed using the exact binomial method (Clopper-Pearson). Analyses were performed using statistical software (SAS EG 4.1 with SAS version 9.1.3). A p value <0.05 was considered statistically significant.

RESULTS

One hundred and twenty-eight women consented to the study. Surgery was completed in 127. Ten major protocol deviations were recorded in 9 patients: 4 patients with POP stage II were inappropriately included and in 6 patients additional prolapse procedures were performed. For analysis of the 3 months results, 9 more patients from a single centre were excluded due to data collection problems, which were resolved prior to collection of the 12-month data (figure 1). Baseline and surgical characteristics are presented in table 1.

Forty-one patients (32.3%) underwent an anterior mesh repair; 16 (12.6%) a posterior repair and 70 women (55.1%) a total pelvic floor repair (total uncut mesh in absence of uterus: 28; total cut mesh in presence of uterus: 42). Anatomic success (POP Stage ≤ I) in the treated compartments at 1 year was 77.4% (95% CI 69.0% - 84.4%). The protocol-defined primary endpoint, based on the per-protocol analysis set, which excluded the 9 patients with a major protocol deviation, yielded a success rate of 78.3% (95% CI 69.6% - 85.4%). When anatomic success was defined as leading edge < 0 cm, the success rate was 89.5% (95% CI 82.7% - 94.3%). Four re-interventions were reported within 1 year following surgery, three in the treated compartment. One patient encountered an immediate recurrence of a stage IV prolapse after a coughing episode during extubation. She was immediately re-operated with a new Prolift +M mesh placement. Despite the fact that this patient demonstrated a successful anatomic result at one year, she was a surgical re-intervention and therefore considered a failure. One patient required a vaginal hysterectomy due to utero-vaginal prolapse following a total, cut mesh repair. Two patients underwent subsequent laparoscopic sacrocolpopexy: one for posterior

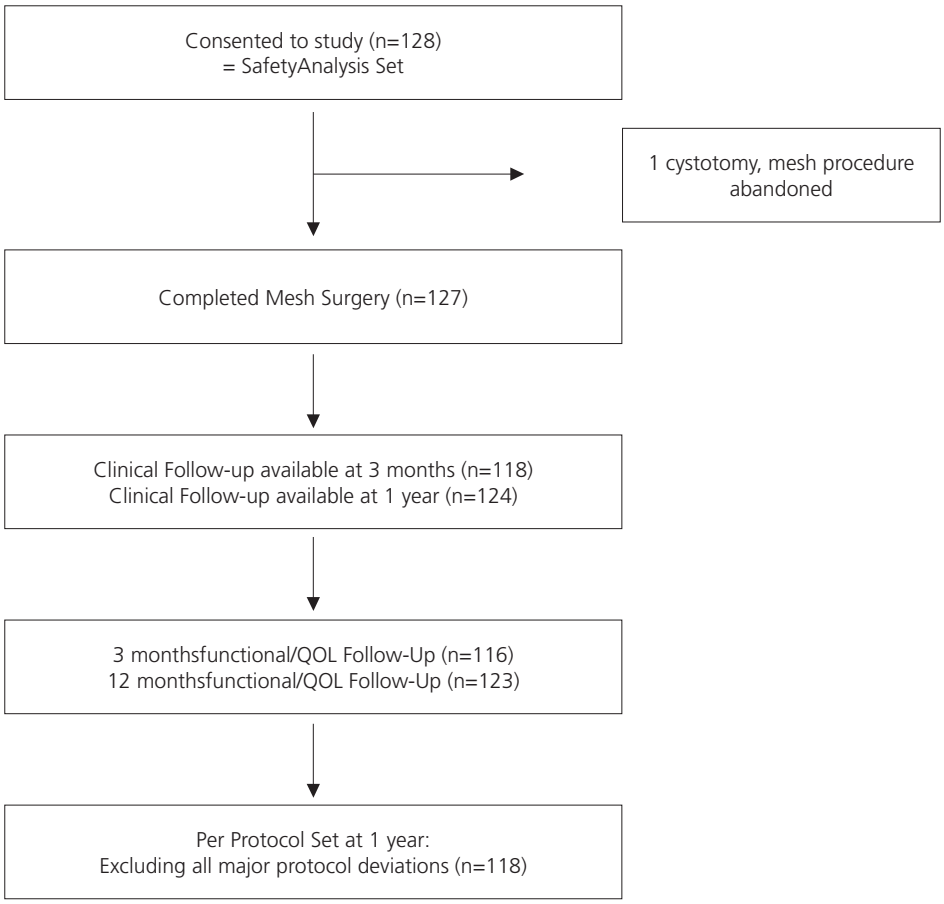

Figure 1. Patients study disposition.

vaginal wall prolapse after total, uncut mesh repair; one for apical failure after an anterior repair. Of 57 patients who had only a single compartment treated, 13 had an untreated stage II prolapse that was not deemed necessary to surgically address. Of 44 patients without prolapse in the other compartment, 9 (20.5%) had developed a de novo stage II prolapse in the untreated compartment by one year. Anatomic results and success rates according to both definitions at 3 months and 1 year are presented in tables 2 and 3.

Significant improvements were observed in all subscales of disease-specific symptoms and QoL scores from baseline compared to 3 months and 1 year (table 4). The mean changes from baseline to 3 months were statistically significant and sustained at 1 year. At baseline 91.2% of patients reported bulge symptoms, compared to 8.9% by one year. Based on the PGI-C, 86.0% of patients indicated their prolapse situation at one year to be "much better."

Table 1. Baseline and surgical characteristics.

Patients	**N: 127**
Mean Age (years)	63.9 (10.1)
Mean BMI kg/m^2	27.5 (3.8)
Median Vaginal deliveries (range)	2 (0-6)
Post-menopausal (n)	117 (92.1%)
Surgical history	
Hysterectomy	52 (40.9%)
Previous POP repair	27 (21.3%)
Previous incontinence surgery	9 (7.1%)
Concomitant procedures	
Hysterectomy	21 (16.5%)
TVT or TVT-O	36 (28.3%)
Perineal repair	14 (11%)
Additional intervention for prolapse	6 (4.7%)
Anesthesia type	
General	80 (63%)
Spinal	47 (37%)

Data presented as means (± standard deviation), median (range) or number (percentage).

Table 2. Anatomical results for the treated compartment at 3 and 12 months.

POP stage	**Baseline (n=127)**	**3 Months (n=118)**	**12 Months (n=124)**
Stage 0	0	68 (57.6%)	51 (41.1%)
Stage I	0	42 (35.6%)	45 (36.3%)
Stage II	4 (3.1%)	7 (5.9%)	24 (19.4%)
Stage III	104 (81.9%)	0	1 (0.8%)
Stage IV	10 (15.0%)	0	0
Re-intervention	-	1 (0.8%)	3 (2.4%)
Success rate % (95% CI)		**93.2 % (87.0 - 97.0)**	**77.4% (69.0 - 84.4)**
Leading Edge	**Baseline (n=127)**	**3 Months (n=118)**	**12 Months (n=124)**
-3 cm	0	70 (59.3%)	54 (43.5%)
-2.5 to -1.5 cm	0	40 (33.9%)	42 (33.9%)
-1 to -0.5 cm	0	1 (0.8%)	15 (12.1%)
0	0	5 (4.2%)	4 (3.2%)
+0.5 to +1 cm	4 (3%)	1 (0.8%)	5 (4.0%)
+1.5 to +2 cm	57 (45%)	0	0
+2.5 to +3 cm	28 (22%)	0	0
>+3 cm	38 (30%)	0	1 (0.8%)
Re-intervention	-	1 (0.8%)	3 (2.4%)
Success rate % (95% CI)		**94.1% (88.2 - 97.6)**	**89.5% (82.7 - 94.3)**

Data presented as numbers (%), CI; confidence interval.

Table 3. Anatomical results in POP-Q measurements.

	All (n=127)		Anterior Repair (n=41)		Posterior Repair (n=16)		Total Repair (n=70)	
	Baseline	**12 months**	**Baseline**	**12 months**	**Baseline**	**12 months**	**Baseline**	**12 months**
Ba	2.4 (2.3)	-2.3 (0.9)**	2.3 (0.7)	-2.3 (0.9)**	-2.0 (0.7)	-2.3 (1.0)	3.4 (1.9)	-2.3 (0.9)**
C	-1.7 (4.5)	-6.5 (2.1)**	-4.9 (2.2)	-7.0 (1.8)**	-3.1 (3.5)	-6.5 (2.1)*	0.4 (4.6)	-6.3 (2.3)**
Bp	0.6 (2.8)	-2.5 (0.8)**	-2.0 (0.7)	-2.1 (1.0)	3.4 (1.5)	-2.4 (1.0)**	1.5 (2.7)	-2.8 (0.4)**
Gh	4.3 (1.0)	3.4 (0.8)**	3.9 (0.9)	3.2 (0.8)**	4.1 (1.0)	3.2 (0.9)*	4.6 (1.0)	3.6 (0.8)**
Pb	2.9 (0.9)	3.2 (0.7)**	3.0 (0.7)	3.2 (0.8)	2.6 (1.0)	2.9 (0.6)	2.9 (1.0)	3.3 (0.7)**
TVL	8.7 (1.3)	8.3 (1.2)**	8.7 (1.4)	8.4 (1.1)	7.6 (1.0)	8.3 (1.2)	8.9 (1.2)	8.2 (1.3)**

POP-Q data presented as mean (± SD). * for p<0.05 and ** for p<0.001. Ba = most dependent point on anterior wall; C = most dependent point of cervix or cuff; Bp = most dependent point of posterior vaginal wall; Gh = genital hiatus; Pb = perineal body; TVL = total vaginal length.

Table 4. Functional results.

All patients n: 127	**Baseline**	**3 months**	**12 months**
PFDI-20	98.9 (52.0)	31.2 (26.4)*	25.9 (28.1)*
POPDI-6	41.4 (21.9)	5.9 (8.2)*	6.3 (9.8)*
CRADI-8	21.6 (17.0)	11.5 (12.3)*	10.4 (13.0)*
UDI-6	35.7 (25.0)	13.8 (17.1)*	9.3 (14.3)*
PFIQ-7	74.5 (70.5)	17.6 (36.5)*	9.3 (23.1)*
POPIQ	24.8 (27.7)	3.8 (12.0)*	1.8 (9.3)*
CRAIQ	18.4 (24.6)	4.7 (13.5)*	3.1 (9.8)*
UIQ	31.3 (27.6)	9.1 (16.6)*	5.6 (13.8)*
PISQ-12 (n=58)	33.4 (7.8)	38.9 (4.9)*	39.0 (4.4)*
PGI-C			
Much better	-	96 (85.0%)	106 (86.2%)
A little better	-	11 (9.7%)	12 (9.8%)
About the same	-	3 (2.7%)	3 (2.4%)
A little worse	-	3 (2.7%)	1 (0.8%)
Much worse	-	-	1 (0.8%)
EQ-5D			
Utility	0.837 (0.161)	0.926 (0.130)*	0.940 (0.114)*
Health state	78.8 (15.7)	86.1 (10.9)*	85.2 (12.5)*

Data presented as mean (± SD) and n (%). PFDI-20 and PFIQ-7 scores range from 0 (best score) to 300 (worst score); POPDI, CRADI, UID, POPIQ, CRAIQ, UIQ scores range from 0 (best score) to 100 (worst score). PISQ-12 scores range from 0 (worst score) to 48 (best score). EQ-5D Utility ranges from 0 (worst score) to 1 (best score) and Health State ranges from 0 (worst score) to 100 (best score). * for p<0.001.

There were large and statistically significant improvements in the EQ-5D Utility and Health State scores from baseline to 3 months and 1 year (table 4).

Sixty-one patients were sexually active at baseline, 58 of whom completed a PISQ-12 questionnaire. At 3 months and 1 year, 48 and 57 patients completed the

questionnaire, respectively. There was a statistically significant improvement in sexual function score in these patients at 3 months, which was sustained at one year, with a mean change in PISQ-12 of 5.2 (SD 6.9; p<0.001) (table 4).

At baseline, dyspareunia was reported in 18/61 (29.5%) sexually active patients. At 1 year, 13 of 17 sexually active patients (76,4%) reported resolution of dyspareunia; 4 had ongoing dyspareunia and 1 patient had not returned to sexual activity for unrelated reasons. There was one report of *de novo* dyspareunia out of 49 (2.0%) patients who reported to be sexually active at 1 year. This patient underwent a total, cut mesh repair and TVT-O sling. There was no mesh exposure. Pain occurred during penetration and was attributed to vaginal dryness. Nine (13.6%) of 66 patients who were not sexually active at baseline, resumed sexual intercourse without reporting *de novo* dyspareunia following surgery (fig 2).

Seven patients (5.5%) reported pelvic pain at baseline during routine activities. By 1 year, there was resolution of this pre-existing pelvic pain in all 7. At 1 year, in 5 (3.9%) patients pelvic pain was reported: 2 during routine daily life, and in 3 patients, pain was only elicited during pelvic examination. These, however, were not present at time of the 3-month assessment. In 2 (1.6%) of the patients reporting pain during pelvic examination, the investigator considered that there was evidence of vaginal wall stiffness. One had an anterior repair and the other total repair; a concomitant retropubic TVT sling was performed in both cases.

A summary of key adverse events is summarized in table 5. Bladder perforation occurred in 3 (2.3%) patients: 1 during dissection, which resulted in the mesh repair being abandoned; another 1 during dissection and 1 as a result of the trocar passage. After repair of the perforation, mesh was placed in the latter two patients. Recovery in these patients was uneventful. Hemoglobin levels dropped 2.2 +/- 1.3 g/dL for total, 1.7 +/- 1.1 g/dL for anterior and 1.0 +/- 0.7 g/dL for posterior repair. One patient who underwent a total repair, required transfusion of 4 units of packed red blood cells. She recovered uneventfully. Thirteen patients had mesh exposure reported over a period of 1 year (10.2%). Eleven of these 13 patients (85%) with mesh exposure underwent a total mesh repair (4 cut, 7 uncut total meshes), the other two were anterior mesh repairs. Seven of these 13 patients had concomitant surgeries: 3 vaginal hysterectomies, 2 mid-urethral slings and 1 perineal repair. The majority of exposures were located at the apex of the vagina (n=6) or on the anterior vaginal wall (n=6); there was one exposure in the posterior wall. Seven patients (54%) underwent partial mesh excision to treat mesh exposure. The remaining six (46%) have been treated successfully with the use of topical estrogen.

COMMENT

This prospective observational multicentre cohort study provides evidence that this partially absorbable mesh used in trans-vaginal mesh surgery results in improved anatomic and functional outcomes at one year in patients with stage III and IV POP.

The major drawback of this study is the lack of a control group, for example with conventional POP surgery. Cohort studies are exposed to selection bias and

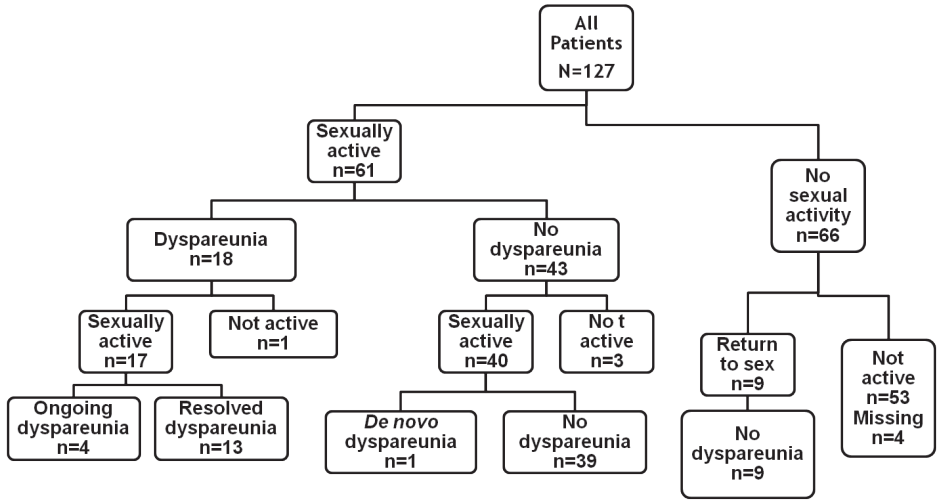

Figure 2. Disposition of sexual function.

Table 5. Complications

Event	N=128
Bladder perforation	3 (2.3%)
Bowel perforation	0
Requirement for transfusions	1 (0.8%)
Pulmonary embolus	2 (1.6%)
Wound infection	2 (1.6%)
Infected hematoma	1 (0.8%)
Temporary urinary retention	1 (0.8%)
Voiding dysfunction	7 (5.5%)
Mesh exposure:	13 (10.2%)
Excised	7 (5.5%)
Conservative treatment	6 (4.7%)
SUI (worsening / *de novo*):	17 (13.3%)
Treated with slings (11); bulking agents (2)	13 (10.2%)
Urge (*de novo*):	1 (0.8%)
Requiring anti-cholinergic treatment	1 (0.8%)

confounding. In this study, no attempt was undertaken to avoid the surgeons' potential bias during follow-up visits or to capture the patients' characteristics that were screened before entry into the trial. Ideally an investigator blinded to the procedure should have performed these. Future preferably randomized, controlled studies are necessary to generate evidence on a risk/benefit analysis of different mesh versus conventional repairs. The strengths of this study on the other hand

are its prospective and international multicentre nature, with the use of validated instruments of measurement, such as POP-Q, PGI-C, PFDI-20, PFIQ-7 and EQ-5D as well as its adequate sample size.

According to strict anatomic outcome criteria the overall anatomic success (POP ≤ stage I) in the treated compartments at 1 year was 77.4% (69.0 - 84.4). The population and results are consistent with similar prospective, multicentre studies reporting 1 year anatomic outcomes, ranging from 79-91%, following POP repair with the original polypropylene mesh in the Prolift system.[14, 16]A decrease in the success rate was observed between the 3 and 12 months follow-up. Other authors have reported similar changes over time. Van Raalte et al reported 94.2% anatomic success at 6 months and 86.6% at 1 year or more after treatment of POP with the Prolift system.[20] A Scandinavian prospective multicentre study on Prolift reported 87-91% success at 2 months, but the same investigators reported 80.6% (74.3-85.7) after 1 year.[14, 29] Furthermore, it might be argued that the absorbable polyglecaprone-25 component, which is added to facilitate handling during surgery, might initially contribute to the graft's strength which could be reflected in the anatomic success rate at 3 months. However, this is unlikely since the material retains only 20-30% of its burst strength after two weeks in vivo, whilst absorption is only complete between 91 and 119 days.[30] In a hernia porcine model light-weight polypropylene mesh with an absorbable monofilament was shown to maintain mean burst strength comparable to medium weight polypropylene, while becoming less stiff than heavier weight meshes after 5 months of tissue incorporation.[31] Another explanation of the difference in anatomic outcome at 3 months and 1 year might be the increased longitudinal elasticity of this lightweight mesh compared to the original Prolift mesh.

Improvements in the leading edge definition of success (leading edge < 0 cm) (89.5%) were consistent with the patient's report of "much better" on the PGI-C global scale (86.2%). The discrepancy between the PGI-C result and the primary definition of success highlights the ongoing debate on the appropriateness of POP stage ≤ I as the ultimate anatomic goal to be achieved in POP repairs. Swift et al demonstrated that POP symptoms clearly correlate with the leading edge of prolapse beyond the hymenal remnants.[32] We therefore agree with Barber et al, who suggested that in future studies on POP surgery, next to anatomic criteria and the absence of reinterventions, the absence of bulge symptoms should be included to determine success.[33]

It is important to note that the differences from baseline in all three subscales in symptoms and QoL, using PFDI-20 and PFIQ-7 questionnaires were significant and sustained over time.

The results from the EQ-5D questionnaire demonstrated that there were significant improvements in utility and health status at 3 months, which continued to 1 year. These values not only indicate good health status and utility improvement of the POP intervention to the patient, but enables comparison to other disease states and future cost-effectiveness analysis of mesh kits. It is worthwhile noting that the improvements seen on the EQ-5D were congruent with the improvements seen on disease-specific questionnaires.

In this study, the rate of de novo dyspareunia was 2.0%, which was encouragingly low compared to previous reports following traditional prolapse repair (14.5-36.1%) and a recent retrospective study reported quoting a similar rate (16.7%) following repair with the original polypropylene mesh.[1, 11, 12]The data of our study suggest a true impact of the new mesh's characteristics on the development of dyspareunia. This might be explained by the increased unidirectional elasticity and reduced fibrotic reaction, allowing adequate vaginal distension, which has been shown to be essential to allow normal sexual intercourse.[34] Accordingly, a significant improvement of 5.2 points in the mean scores of the PISQ-12 was found in this study. Contrariwise, a previous study on sexual function one year after Proliftrepair reported adecline in mean PISQ-12 score of 3-4 points.[35] The improved sexual function observed in this study therefore is encouraging and warrants further evaluation in well designed comparative studies, with sexual function and de novo dyspareunia as primary outcomes.

The rate of vaginal wall stiffness at one year was 1.6%. This study prospectively evaluated vaginal wall stiffness, which currently still is a subjective measurement based on clinician judgment. Identifying a reliable and reproducible objective measure of vaginal wall stiffness will be of importance in future studies to evaluate the effects of mesh, as well as conventional POP repairs on the physical characteristics of the vaginal wall and any associated adverse effects. The low rate of de novo pelvic pain and vaginal wall stiffness was reassuring. This observation could be related to a reduced surface area of this mesh, which would have lead to a reduction in fibrotic reaction around the individual mesh fibres, resulting in the formation of a scar net rather than a scar plate.[31]

This observational series with this partially-absorbable light-weight mesh did not demonstrate a difference in mesh exposure rate compared to procedures using the original mesh, which could have been expected based on preclinical data of animal studies.[17, 31] The safety profile was comparable to the original mesh repairs.[13, 14, 16]

The results of this study are suggestive that this lightweight mesh provides anatomic support consistent with the original polypropylene mesh, and demonstrate high functional improvements. No apparent safety concerns appeared from the change in mesh. The low rate of de novo dyspareunia together with the absence of clinically relevant mesh shrinkage is particularly encouraging. Longer-term evaluation of this lightweight mesh continues.

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6

SEXUAL FUNCTION FOLLOWING TROCAR-GUIDED MESH OR VAGINAL NATIVE TISSUE REPAIR IN RECURRENT PROLAPSE *A RANDOMIZED CONTROLLED TRIAL*

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ABSTRACT

Introduction

Surgical treatment of pelvic organ prolapse (POP) affects sexual function. Generally this results in improved sexual function, but deterioration is reported also.

Aim

The purpose of this study was to evaluate and compare sexual function in patients with recurrent POP undergoing either a vaginal surgical repair with native tissue or a trocar-guided mesh insertion.

Main Outcome Measures

Primary outcome was sexual function at 12 months following surgery, measured by the short form of the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12). Secondary outcomes were the identification of factors independently associated with change in PISQ-12 scores and changes in individual PISQ-12 question scores.

Methods

Sexually active patients randomly assigned to either native tissue repair or trocar-guided mesh insertion, which had completed the PISQ-12 both at baseline and at 12 months, were included. Total, subscale and individual question analysis was performed. Logistic regression was used to identify factors that were independently associated with improvement/deterioration in total PISQ-12 scores.

Results

Sixty patients were included; 32 in the mesh arm and 28 in the native tissue arm. At 12 months PISQ-12 scores were not different in both treatment arms (34.3, S.D 6.7 vs. 34.7, S.D 5.7), but improvement was detected in the native tissue arm, whereas PISQ-12 total score remained unchanged in the mesh arm. Deteriorations were observed in the behavioral/emotive subscale and partner related items in the mesh arm. In the native tissue arm significant improvements in the physical and partner related subscales were observed. The presence of mesh exposure was independently associated with deterioration in total PISQ-12 score.

Conclusion

At 12 months PISQ-12 scores were not different in either treatment arm, but were affected differently by trocar-guided mesh insertion or by native tissue repair. Mesh exposure was independently associated with deterioration in sexual function.

INTRODUCTION

Pelvic Organ Prolapse (POP) is a common problem and may occur in up to 50% of parous women.[1] A large Dutch cross-sectional study demonstrated a prevalence of symptomatic POP as high as 11.4%.[2] The frequently cited study by Olsen et al, in which a lifetime risk of undergoing a prolapse or urinary incontinence operation in the U.S of 11.1% was reported, has been replicated, whereby the initial estimate could be confirmed with a lifetime risk of 11.8%.[3, 4] Recently, Australian authors calculated that the risk of surgery for POP in the general female population of Western Australia was as high as 19%.[5] The high likelihood of undergoing surgery for POP combined with known anatomic failure rates for native tissue repairs that range between 30-70% for the anterior vaginal wall and around 20% for the posterior vaginal wall, have led to increased use of prosthetic mesh in vaginal POP surgery with the aim to reduce failure rates and increase durability.[6-9]

The use of these materials has introduced new kinds of morbidity, such as mesh exposure and contraction of tissue around the mesh.[10] These may result in pelvic pain and dyspareunia.[11] Sexual function may be adversely affected by these problems, but the presence of POP has adverse effects on sexual function as well, although data on this association are somewhat conflicting.[12-15] Rogers et al have developed a condition specific, validated and self-administered questionnaire to evaluate sexual function in women with POP and/or urinary incontinence, of which the short form is the PISQ-12.[16] This instrument has been used in studies evaluating sexual function after surgery for pelvic floor dysfunction, with increased postoperative PISQ scores in around 70%.[14] Recently, deterioration in sexual function has been reported following the use of synthetic mesh kits for the repair of POP.[17, 18]

Aims

The purpose of this study was to evaluate and compare sexual function measured by the PISQ-12 in women undergoing surgery for recurrent POP one year after either a vaginal native tissue repair or surgery with a commercially available mesh kit.

METHODS

This study is a secondary analysis of data from patients of a multicenter randomized controlled trial that primarily aimed to compare anatomic outcomes of the treated vaginal compartments in patients with recurrent POP, who were randomly assigned to either a conventional vaginal native tissue repair or to a tension free vaginal mesh insertion with a commercially available mesh kit (Prolift™, Ethicon, Somerville, NJ, USA).[19] Native tissue repair surgery was performed according guidelines described in that trial. The mesh procedure was performed as described by Fatton et al.[20]

Patients were included in the present study if they were sexually active and had completed the PISQ-12, both at baseline and at 12 months following surgery.[16] Patients were considered to be 'sexually active' if they answered 'yes' to the question; 'Are you having sexual contact with your partner?' PISQ-12 individual question scores range from 0 (never) to 4 (always) according a five point Likert scale. Total PISQ-12

scores range from 0, which represents poorest sexual function, to 48, best sexual function. A questionnaire was considered valid if there were no more than 2 missing items.[16] Patients, who completed only one questionnaire, either at baseline or at 12 months, were excluded, but included in a missing data analysis.

Baseline evaluation included medical history, physical and gynecological examination and a Pelvic Organ Prolapse Quantification (POP-Q), as well as the completion of the self-administered standard Dutch urogynecological questionnaire, that contains the validated Dutch versions of the Urogenital Distress Inventory (UDI), the Defecatory Distress Inventory (DDI) and the Incontinence Impact Questionnaire (IIQ) and PISQ-12.[16, 21-23] The validated American English version of the PISQ-12 was translated into Dutch, underwent cultural adaption in accordance with the International Society of Pharmacoeconomics and Outcomes (ISPOR) and was back translated.[24] At 12 months POP-Q examinations were repeated and patients were requested to complete these questionnaires once more.

Main outcome measures

Primary outcome of this study was sexual function at 12 months following POP surgery and changes (improvement/deterioration) in sexual function scores measured by the PISQ-12. Secondary outcomes were the identification of factors that were independently associated with these changes and changes in individual PISQ-12 question scores.

Sample size calculation was based on an estimated difference of 10 points in PISQ-12 scores between the two treatment groups at 12 months, assuming an average decline of 5 points for the mesh group and an estimated equal rise for the native tissue repair group. To detect this difference with a power of 80% 30 patients were needed in each group.[17, 18, 25] To objectify the clinical relevance of statistically significant changes in PISQ-12 scores we calculated effect sizes, using Cohen's d. Effect sizes (E.S) are defined as small if Cohen's d=0.2, medium if d=0.5 and large if $d \geq 0.8$.[26]

To compare mean continuous data within groups paired samples t-tests were used and for comparison between groups independent samples t-tests. For numbers smaller than 30 and comparison within groups Wilcoxon signed rank test was used and for comparison between groups Mann-Whitney U test. To compare categorical variables Pearson's Chi-square was used, and for numbers smaller than 5 Fisher exact test. Improvement in PISQ-12 score was defined as a postoperative score at least one point higher than the pre-operative score, deterioration as a postoperative score at least one point lower than the pre-operative score. Logistic regression was used to identify factors that were associated with either improvement or deterioration in total PISQ-12 scores. Covariariables with a $p<0.3$ were entered in a multivariable logistic analysis model using Method Forward Wald. P-values <0.05 were considered statistically significant. Statistical analysis was performed using Statistical Package for the Social Sciences, version 18.0 (SPSS Inc.,Chicago,Ill.,USA).

RESULTS

One hundred and ninety-four patients with recurrent POP were enrolled and randomly assigned to either a Prolift™ or a conventional vaginal POP repair. Ninety-three patients underwent Prolift™repair and 97 a native tissue repair between June 2006 and July 2008. Fifty-four of 78 (69%) and 50 of 76 (66%) patients in the mesh arm and native tissue arm respectively were considered 'sexually active'. Sixty patients completed a PISQ-12 both at baseline and 12 months. Of those 32 underwent Prolift™repair and 28 a native tissue repair. Thirty-one and 27 patients, in the mesh and native tissue arm respectively, completed only one PISQ-12, either at baseline or at 12 months. They were considered 'incomplete responders'.

Table 1 shows some baseline, clinical, surgical and anatomic outcome characteristics of the 60 study patients. Patients did not differ in age, perceived general health (mean VAS-score), BMI, parity, amount of co morbidity, or prior (POP) surgery. In both treatment arms one hematoma was recorded and treated conservatively. In the mesh arm two patients had a bladder perforation that occurred during dissection. In both cases the perforation was repaired and mesh inserted. In the mesh arm 11 of 32 patients (34%) were diagnosed with a mesh exposure detected between six weeks and 12 months postoperatively. Overall POP stages for both groups at baseline and 12 months are shown. Anatomic improvements, in terms of stage of leading edge of prolapse were significant, but not different between groups. Anatomic successes, defined as overall POP stage ≤I were equal: 15 of 32 (47%) patients in the mesh arm and 13 of 28 (46%) in the native tissue repair arm. Highly significant improvements in UDI domain score of prolapse were observed in both arms. No differences between groups were observed in UDI, DDI and IIQ domain scores at baseline (not shown), except for the UDI domain of pain, that scored significantly higher (worse) in the native tissue arm; 29.9 (27.3) vs. 16.7 (22.4) respectively (p 0.048).

In table 2 mean total and subscale PISQ-12 scores are shown at baseline and 12 months. No significant differences in total PISQ-12 scores were observed at 12 months between groups, but there were differences in total PISQ-12 score at baseline. A significant improvement in PISQ-12 score was observed in the native tissue repair group that could be particularly attributed to significant improvements in the physical (E.S 0.68, p 0.002) and partner-related (E.S 0.62, p 0.018) subscales. In contrast with this improvement, a significant and clinically relevant deterioration in the behavioral/emotive subscale (E.S 0.34, p 0.012) was observed in the mesh arm.

Table 3 shows the results of individual PISQ-12 question scores. Significant declines in the frequency of orgasm (E.S 0.42, p 0.018) and being sexually excited were observed in patients of the mesh group (E.S 0.47, p 0.006). An increase in problems related to erectile function of the male partners was observed in this group as well (E.S 0.38, p 0.032). Avoidance of sexual intercourse because of bulge symptoms decreased in both arms, but with a larger effect size in the conventional arm (E.S 0.91, p 0.002 vs. 0.43, p 0.028). The intensity of orgasms increased significantly in the native tissue repair group (E.S 0.46, p 0.017). Neither in the mesh, nor in the native tissue repair arm significant changes post- to preoperatively were recorded in pain during sexual intercourse.

Table 1. Baseline, clinical, surgical characteristics and anatomical outcomes

				Prolift™ N: 32	**Native tissue repair N: 28**	**P**	
Age (years)				59.5 (8.6)	62.0 (8.2)	0.260*	
VAS general health (0-100)				78.0 (9.5)	70.6 (18.8)	0.063*	
BMI				26.4 (2.4)	25.3 (2.4)	0.081*	
Parity				2 (1-4)	2 (1-3)	0.437^	
Comorbidity				10 (31%)	7 (25%)	0.591†	
POP repair surgery							
Anterior Prolift™				15 (46%)	-		
Posterior prolift™				12 (38%)	-		
Total Prolift™				5 (16%)	-		
(Concomitant) POP surgery				3 (9%)	-		
Vaginal hysterectomy				0	1		
Anterior colporrhaphy				1	14		
Posterior colporrhaphy				1	14		
Perineoplasty				0	2		
Manchester Fothergill				1	2		
Enterocele repair				0	2		
Sacrospinous fixation				0	7		
Uterosacral ligament suspension				0	1		
Complications							
Bladder perforation				2	0	0.500	
Hematoma				1	1	1.000	
Cumulative Mesh Exposure				11 (34%)	0	<0.001	
Outcomes		**Baseline**		**12 months**	**Baseline**	**12 months**	
Overall† POP	Stage ≤ I	-		**15(47%)**	-	**13(46%)**	
	Stage II	17(53%)		16(50%)	14(50%)	15(54%)	
	Stage III	14(44%)		1(3%)	13(46%)	-	
	Stage IV	1(3%)		-	1(4%)	-	
UDI Pain		**16.7**(22.4)	7.3(15.2)	p 0.020#	**29.9**(27.3)	16.0(23.3)	p 0.020#
UDI Prolapse		48.9(34.9)	8.1(20.6)	p<0.001	47.3(30.0)	5.3(15.7)	p <0.001

Data presented as mean (SD) or numbers (percentage).
*Independent samples t test, ^ Mann-Whitney U test, other p values: Pearson Chi square or Fisher exact in case of small numbers. † POP stage of the leading edge of prolapse. ## Fisher exact test, # Paired samples t test.
Baseline difference UDI Pain between groups p 0.048 (independent samples t test).

Table 2. PISQ-12 total and subscale scores at baseline and 12 months post surgery

		Prolift™ repair N: 32				Native tissue repair N: 28			
PISQ-12 total score		**Baseline**	**12 months**	**Change**	**Effect size**	**Baseline**	**12 months**	**Change**	**Effect size**
Total score		35.0 (5.7)	34.3 (6.7)	-0.7 (4.7)	-	31.5 (7.2)	34.7 (5.7)	**+3.2 (6.7)**	0.49
Percentiles	25	32.00	30.50	P 0.418		26.25	30.25	**P 0.017**	
	50	35.00	35.00	(0.549[a])		31.50	35.00	(0.007[a])	
	75	40.00	39.75			38.00	38.50		
PISQ-12 subscale scores									
Behavioral/emotive		13.8 (3.1)	12.5 (3.9)	-1.2 (2.6)	0.34	12.5 (3.9)	12.7 (3.5)	+0.2 (3.4)	-
				P 0.012 (0.009[a])		p 0.160[†]	p 0.834[#]	p 0.744 (0.626[a])	
Physical		13.1 (3.1)	13.8 (2.4)	+0.7 (2.0)	-	11.8 (2.3)	13.3 (2.1)	+1.5 (2.2)	0.68
				P 0.068 (0.074[a])		p 0.069[†]	p 0.393[#]	**P 0.002** (0.003[a])	
Partner related		8.0 (1.9)	7.8 (2.2)	-0.2 (1.8)	-	7.8 (1.9)	8.7 (1.6)	+0.9 (1.8)	0.62
				P 0.561 (0.470[a])		p 0.685[†]	p 0.073[#]	**P 0.018** (0.017[a])	

Data presented as mean (SD). P: paired samples t-test. [a] Wilcoxon signed rank test (to compare p-values for means of n<30), p[†] for differences between groups at baseline (p 0.040[†] for total score), p[#] for differences between groups at 12 months (p 0.982[#] for total score at 12 months), both independent samples t-test. Bold values are statistically significant. Effect sizes (E.S) were calculated for statistically significant differences; E.S is defined small if Cohen's d = 0.2, medium d = 0.5, large if d ≥ 0.8. **Bold** values are statistically significant (P<0.05).
Valid questionnaires: questionnaires with a maximum of 2 missing items.
Behavioral/emotive subscale: Questions 1,2,3,4 and 9 (desire, arousal, emotions). Physical subscale: Questions 5,6,7 and 8 (pain, urinary and/or fecal incon-tinence and bulge symptoms). Partner related subscale: Questions 10,11 and 12 (erection, premature ejaculation and intensity of orgasm).

Table 3. PISQ-12 individual question scores at baseline and 12 months post surgery

PISQ-12 individual question scores	Prolift™ repair N: 32				Native tissue repair N: 28			
	Baseline	12 months	P	Effect size	Baseline	12 months	P	Effect size
Q1. How frequently do you feel sexual desire? This feeling may include wanting to have sex, planning to have sex, feeling frustrated due to lack of sex, etc.								
	2.0 (0.8)	2.0 (0.9)	0.625 (0.617[a])	-	1.9 (2.0)	2.0 (0.7)	0.477 (0.467[a])	-
Q2. Do you climax (have an orgasm) when having sexual intercourse with your partner?								
	2.7 (1.2)	2.2 (1.2)	**0.018** (0.018[a])	0.42	2.2 (1.1)	2.1 (1.2)	0.541 (0.582[a])	-
Q3. Do you feel sexually excited (turned on) when having sexual activity with your partner?								
	2.8 (0.8)	2.4 (0.9)	**0.006** (0.003[a])	0.47	2.5 (1.1)	2.4 (1.1)	0.702 (0.805[a])	-
Q4. How satisfied are you with the variety of sexual activities in your current sex life?								
	2.9 (1.0)	2.6 (1.2)	0.095 (0.090[a])	-	2.8 (1.0)	2.7 (1.1)	0.745 (0.935[a])	-
Q5. Do you feel pain during sexual intercourse?								
	3.1 (1.1)	3.0 (1.2)	0.488 (0.457[a])	-	1.9 (1.1)	2.4 (1.4)	0.070 (0.072[a])	-
Q6. Are you incontinent of urine (leak urine) with sexual activity?								
	3.5 (1.1)	3.6 (1.0)	0.325 (0.317[a])	-	3.6 (0.6)	3.7 (0.6)	0.537 (0.527[a])	-
Q7. Does fear of incontinence (either stool or urine) restrict your sexual activity?								
	3.6 (1.1)	3.8 (0.5)	**0.032** (0.038[a])	0.24	3.6 (1.0)	3.6 (0.9)	0.574 (0.589[a])	-
Q8. Do you avoid sexual intercourse because of bulging in the vagina (either the bladder, rectum or vagina falling out)?								
	3.0 (1.2)	3.5 (1.1)	**0.027** (0.028[a])	0.43	2.5 (1.5)	3.6 (0.8)	**0.001** (0.002[a])	0.91
Q9. When you have sex with your partner, do you have negative emotional reactions, such as fear, disgust, shame or guilt?								
	3.4 (1.1)	3.5 (1.0)	0.690 (0.751[a])	-	3.1 (1.2)	3.5 (0.8)	0.125 (0.133[a])	-
Q10. Does your partner have a problem with erections that affects your sexual activity?								
	3.2 (1.0)	2.8 (1.1)	**0.032** (0.037[a])	0.38	3.1 (1.1)	3.4 (1.0)	0.229 (0.242[a])	-
Q11. Does your partner have a problem with premature ejaculation that affects your sexual activity?								
	3.5 (0.8)	3.3 (0.9)	0.083 (0.083[a])	-	3.4 (0.8)	3.6 (0.8)	0.110 (0.124[a])	-
Q12. Compared to orgasms you have had in the past, how intense are the orgasms you have had in the past six months?								
	1.3 (1.0)	1.7 (1.0)	0.070 (0.062[a])	-	1.2 (1.0)	1.6 (0.7)	**0.016** (0.017[a])	0.46

Data presented as mean (SD), P: paired samples t-test. In second column: [a] Wilcoxon signed rank test (to compare p-values for means of n<30), **Bold** values are statistically significant (P<0.05). Effect size; small if Cohen's d = 0.2, medium d = 0.5, large if d ≥ 0.8.

Table 4 shows results of univariable and multivariariable logistic regression analysis for factors expected to be associated with change in total PISQ-12 scores.[27, 28] A native tissue repair as compared to a mesh repair appeared to be independently associated with improvement in PISQ-12 scores with an odds ratio (OR) of 4.6 (95%CI 1.4-15.2, p 0.012). On the other hand the presence of a mesh exposure was independently associated with deterioration of PISQ-12 scores (OR 7.8; 95%CI 1.5-41.0, p 0.015).

Table 5 shows the results of the missing data analysis. No significant differences could be detected between full and incomplete responders, except for two items. At baseline a statistically significant higher score in the IIQ domain embarrassment was observed in the incomplete responders group. The presence of mesh exposures on the other hand was overrepresented in the full responders group (11 of 32, 34% vs. 2 of 31, 6%; p 0.005).

DISCUSSION

In this study we observed no significant differences in total PISQ-12 scores at 12 months between patients who had been treated with trocar-guided mesh insertion or by vaginal native tissue repair of POP. However, in contrast with the mesh arm, we observed improvements of sexual function in patients treated by native tissue repair, which could be entirely attributed to improvements in the physical and partner related domains, while the behavioral/emotive subscale remained unchanged. Likewise, Rogers et al previously had reported higher PISQ scores in 70% of women 3 to 6 months following conventional surgery for POP and/or urinary incontinence (UI), as a result of improvements of the physical and partner-related domains, while the behavior/emotive domain showed no change.[28] Other authors reported comparable results after treatment for stress UI and abdominal sacrocolpopexy.[29, 30]

In contrast with these reports we noticed that subtle improvements in the physical subscale of patients in the mesh arm were nullified by a significant deterioration of the behavioral/emotive subscale. More recent studies on mesh and its effect on sexual function do show a differentiated picture. Sentilhes et al reported no change in PISQ-12 scores at one year following transvaginal POP repairs with a variety of non-absorbable meshes in a group of 37 sexually active women.[31] However, Altman et al reported significant deteriorations of PISQ-12 scores, with a mean of almost 4 points, at one year following trocar-guided transvaginal mesh repairs, which were entirely attributed to worsening in the behavioral/emotive and partner-related items.[17] Su et al reported an even greater average decline of 10 points in PISQ-12 scores, caused by deteriorations in all three subscales, of 33 patients, 6 months after a Prolift procedure.[18]

Searching for the rationale of the lack of improvement in total PISQ-12 scores in the mesh arm and more in particular the deterioration of the behavior/emotive subscale we propose the following possible explanation. This type of non-absorbable mesh is known for its inherent fibrosis and potentially considerable contraction of tissue around the mesh.[10, 32] Insertion of this type of mesh possibly impairs vaginal compliance and thereby the physiological response to sexual stimuli. Sexual arousal normally results in

Table 4. Logistic regression analysis for factors associated with PISQ-12 improvement and deterioration.

a. Improvement in PISQ-12 score	Yes N: 31	No N: 29	Univariable analysis OR (95% CI)	P	Multivariable analysis Adjusted OR (95% CI)	P
Age (years)	61.1 (8.3)	60.2 (8.7)	1.012 (0.952-1.076)	0.694		
VAS general health	74.5 (16.8)	74.7 (12.8)	0.999 (0.964-1.035)	0.952		
BMI	25.6 (2.7)	26.2 (2.1)	0.900 (0.615-1.316)	0.586		
Overall POP stage ≥ II	14 (45%)	18 (62%)	0.503 (0.179-1.411)	0.192		0.341
Native tissue versus Prolift™repair	19 (61%)	12 (39%)	3.519 (1.209-10.240)	**0.021**	**4.608 (1.393-15.151)**	**0.012**
Mesh exposure	2 (6%)	9 (31%)	0.142 (0.027-0.745)	**0.021**		0.110
b. Deterioration in PISQ-12 score	**Yes N: 27**	**No N: 33**	**Univariable analysis OR (95% CI)**	**P**	**Multivariable analysis Adjusted OR (95% CI)**	**P**
Age	60.4 (8.9)	60.9 (8.1)	0.992 (0.933-1.055)	0.796		
VAS general health	75.6 (12.3)	73.8 (16.8)	1.008 (0.972-1.046	0.658		
BMI	26.2 (2.1)	25.6 (2.7)	1.112 (0.760-1.626)	0.586		
Overall POP stage ≥ II	16 (59%)	16 (48%)	1.545 (0.533-4.317)	0.406		
Prolift™ versus native tissue repair	19 (70%)	8 (30%)	3.654 (1.239-10.777)	**0.019**		0.183
Mesh exposure	9 (33%)	2 (6%)	7.800 (1.485-40.971)	**0.019**	**7.800 (1.485-40.971)**	**0.015**

Data presented as mean (SD), VAS general health at baseline: scores range from 0 (worst imaginable health) to 100 (best imaginable health).
OR Odds Ratio (95% Confidence Interval). Covariables with a p<0.3 were entered in a multivariate logistic model using Method Forward Wald.
Bold values are statistically significant (P<0.05).

congestion and vaginal wall thickening, tenting and lubrication.[33, 34] A recent study on a partially absorbable and more flexible mesh, in an otherwise identical trocar-guided mesh kit, demonstrated significant increases in overall PISQ-12 scores.[35] To our opinion, these findings do support the hypothesis that a mesh that causes less fibrosis and tissue contraction facilitates a more physiological sexual response of the vaginal wall.

Another explanation for the unequal changes in PISQ-12 scores between the two treatment arms could be the difference in altered body image after the two surgical procedures. Lowenstein et al recently reported that PISQ-12 scores were not related to stage or compartment of POP, but to a woman's self-perceived body image and degree of bother from POP.[36] Lowder et al reported improved body image and sexual function following a variety vaginal and abdominal POP repairs.[37] The authors however did not report on a sub analysis of vaginal mesh and non-mesh repairs.

Table 5. Comparison of full and incomplete responders.

Baseline data		***Full Responders*** *N: 60*	***Incomplete Responders*** *N: 58*	**P**
Age (years)		60.7 (8.4)	59.3 (9.8)	0.411
VAS general Health		74.6 (14.8)	76.5 (16.2)	0.553
BMI		26.6 (4.2)	27.6 (6.7)	0.405
Overall POP	Stage II	31 (52%)	32 (55%)	0.702*
	Stage III	27 (45%)	22 (38%)	0.533*
	Stage IV	2 (3%)	4 (7%)	0.378**
Prolift™ repair		32 (53%)	31 (53%)	0.990
Mesh exposure		11 (34.4%)	2 (6.4%)	**0.005****
Native tissue repair		28 (47%)	27 (47%)	0.990
UDI OAB		29.6 (28.6)	32.1 (25.8)	0.512
UDI Incontinence		19.0 (21.7)	21.9 (21.5)	0.492
UDI Obstructive micturition		25.1 (28.4)	22.5 (27.7)	0.628
UDI Pain		22.6 (25.1)	28.5 (24.1)	0.235
UDI Genital prolapse		47.4 (32.8)	55.9 (32.0)	0.208
DDI Constipation		13.7 (17.4)	10.1 (18.4)	0.324
DDI Obstructed defecation		16.2 (19.5)	11.7 (13.3)	0.169
DDI Pain		10.4 (19.3)	7.6 (16.1)	0.413
DDI Incontinence		7.3 (13.9)	10.5 (22.0)	0.391
IIQ Physical functioning		20.5 (24.0)	27.9 (29.7)	0.170
IIQ Mobility		23.2 (24.0)	29.0 (26.2)	0.236
IIQ Social functioning		14.9 (18.7)	20.8 (18.5)	0.108
IIQ Embarrassment		9.5 (14.5)	18.1 (22.7)	**0.030**
IIQ Emotional Health		18.5 (20.5)	22.9 (24.0)	0.319
PISQ-12 score baseline		33.4 (6.6)	30.6 (6.4) (n: 15)	0.147
PISQ-12 score 12 months		34.5 (6.2)	33.1 (6.6) (n: 43)	0.478

Data presented as mean (SD), VAS score: 0-100.p-value: independent samples t test, * Pearson's Chi square test, ** Fisher exact test. **Bold** p-value is statistically significant.

Last but not least, the role of the male sexual partner is unclear and rather underexposed in the literature on sexual function and POP surgery. Improved female sexual function, measured with the Female Sexual Function Index, has been reported in patients following a vaginal native tissue POP repair with simultaneously increased interest, sexual drive and overall satisfaction by their male partners.[38] It is imaginable that the awareness of a mesh-reinforced vaginal repair by the male partner makes him to be more reluctant and thoughtful in sexual engagement with his wife, which could possibly affect his sexual interest, which in return could be perceived by her as an increase in problems with erectile function of her partner. Furthermore we found the presence of a mesh exposure to be independently associated with deterioration in PISQ-12 score. The awareness of such a mesh exposure could at least be another reason for diminished sexual interest, arousal and consequently erectile function of the male partner. Seven of the 11 mesh exposure patients and their partners were aware of these before completing the 12-months questionnaires. This could be a cause of sexual distress. The psychological awareness of such a mesh exposure could therefore have had impact on the way these patients answered the PISQ-12 questions.[15]

Remarkably, increase of pain during sexual intercourse following trocar-guided mesh surgery, as has been reported by others, was neither observed in this nor in previous work by us and is comparable with results of Altman et al.[17, 39, 40]

Strengths of this study are its randomized controlled design and the use of validated instruments of measurement. Computation of effect sizes contributed to the unraveling of the clinical relevance of statistical significant findings.[26]

On the other hand this study is subject to several limitations as well. To start, patients in the native tissue arm demonstrated lower PISQ-12 scores at baseline compared with patients in the mesh arm. Recently normative values for the PISQ-12 have been established in a general female, sexually active population. A normative score of 40 was suggested for sexually active women without bothersome POP or UI. Women, bothered by POP or UI, showed a mean score of 36 (±5.6), women with depressive symptoms and POP had lower mean scores (33.1±5.7) and women who scored high on a pelvic Pain and Urgency/Frequency scale scored significantly lower than women without these symptoms (30.9±6.5).[25] The latter seems plausible as explanation for the lower PISQ-12 scores at baseline for patients in the native tissue arm, since they scored significantly higher on the UDI domain of pain at baseline than patients in the mesh arm (table 2). Despite clear entry criteria of the original study the randomization procedure, which was generated by a central computer, could not prevent that this difference in baseline characteristic occurred.[19] Secondly, the group of incomplete responders was rather large. A missing data analysis however, revealed no significant differences between complete and incomplete responders, except for inequality in the percentage of mesh exposure and the domain score of embarrassment of the IIQ. This could explain some of the reluctance of these patients to complete an intimate sexual function questionnaire.

Explanations for the lack of difference in total PISQ-12 scores between groups at 12 months could be the equality of overall anatomic outcome for either treatment

arm, the relative high number of patients with a mesh exposure in the mesh arm or the lack of power of the study to detect a difference. We would be able to detect a difference of 10 points (assuming an average decline of 5 for the mesh arm (33→28) and a similar rise of 5 (33→38) for the conventional arm) with a power of 80%, given the a priori sample size of 30 for each arm (α 0.05, β 0.20).[17, 18, 25] For differences smaller than 10 points, the chance of a type II error increases. Furthermore, the PISQ-12 might not be sensitive enough to capture all delicate changes in sexual function following POP repair with or without mesh.[41]

In conclusion we found no difference in PISQ-12 scores at 12 months between the two types of vaginal surgery. Overall sexual function did not improve following trocar-guided mesh insertion, in contrast with native tissue repair and was affected differently. Mesh exposure appeared to be independently associated with deterioration in PISQ-12 scores. Future research on POP and sexual function should also incorporate body image and male aspects of sexual function.

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7

OUTCOMES & PREDICTORS OF FAILURE OF TROCAR-GUIDED VAGINAL MESH SURGERY FOR PELVIC ORGAN PROLAPSE

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ABSTRACT

Objectives

To compare one-year conventional and composite outcomes of trocar-guided vaginal mesh surgery and identification of predictors of failure.

Study design

Prospective observational Cohort study. Failure outcome definitions were: I; prolapse stage ≥ II in mesh treated compartments, II; overall prolapse stage ≥ II, III; composite outcome of overall prolapse > hymen *and* presence of bulge symptoms *or* re-surgery. Logistic regression to identify predictors of failure.

Results

One-year follow-up of 433 patients. Treated compartment failure (I): 15% (95% CI 12-19). Overall prolapse failure(II): 41% (95% CI 36-45). Composite failure (III): 9% (95% CI 7-13). Predictor of failure in all outcomes: combined anterior/posterior mesh with the uterus in situ.

Conclusion

Outcome of prolapse surgery depends on outcome definition. The mesh treated compartment failure outcome (I) and the composite failure outcome (III) appeared not to be statistically different. Consistent factor for failure in all outcomes was the combined anterior/posterior mesh insertion with the uterus in situ.

INTRODUCTION

Pelvic Organ Prolapse (POP) may occur in up to 50% of parous women.[1] The lifetime risk of undergoing surgery for POP in the general female population to the age of 85 has recently been reported to be as high as 19-20%.[2, 3] This high likelihood of undergoing surgery for POP combined with the knowledge of anatomic failure rates for native tissue repairs that range between 30-70% for the anterior vaginal wall and around 20% for the posterior vaginal wall, have led to the increased use of prosthetic mesh in vaginal prolapse surgery with the main aim to reduce anatomic failure rates and increase the durability of repairs.[4-9] Most studies have used strict anatomic outcome criteria as proposed by the National Institutes of Health (NIH) Workshop on Standardization of Terminology for Researchers in Pelvic Floor Disorders in 2001, and only used patient reported outcomes as a secondary outcome measure.[10, 11] But recently Barber et al have demonstrated that the postoperative absence of vaginal bulge symptoms had a significant relationship with a patient's assessment of overall improvement, while anatomic success alone did not.[12] The authors therefore suggested that any future definition of success of POP surgery should include the absence of bulge symptoms in addition to anatomic criteria and the absence of re-treatment. The authors agreed with Swift et al that the hymen should thereby be regarded as the threshold for anatomic success.[12, 13]

The primary objective of this study was to compare one-year outcomes of a large cohort of patients that underwent trocar-guided tension-free vaginal mesh surgery (Prolift™, Ethicon, Somerville, NJ, USA) according to the conventional NIH Workshop criteria with the newly suggested composite outcome of Barber et al.[12] The second objective was to identify possible predictors of failure for these outcomes.

MATERIALS AND METHODS

This prospective observational cohort study is part of an ongoing outcome quality registration project of Radboud University Medical Centre the Netherlands, which has been approved by CMO Arnhem-Nijmegen, April 2006. The present analysis includes 12-month follow-up data of consecutively performed trocar-guided tension--free vaginal mesh procedures (Prolift, Ethicon) between September 2005 and April 2010. Details of 150 patients in this cohort have previously been reported in a study focusing on de novo prolapse in untreated vaginal compartments, and 93 were part of a randomized controlled trial, comparing mesh with native tissue repair in recurrent prolapse.[8, 14]

Inclusion criteria were increased risk of recurrence, which was considered recurrent pelvic organ prolapse stage II or higher or primary pelvic organ prolapse stage III or higher.[8, 15, 16] Exclusion criteria were (contemplating) pregnancy or a compromised immune system.

Surgery was performed by17 gynecologists in 13 collaborating centers. The range of procedures varied from 1 to 209 (mean: 25, median: 3). Four performed more than 25 procedures. All gynecologists were trained for the tension-free vaginal mesh

procedure as described by Fatton et al.[17] Depending on the prolapsed compartment, mesh insertion could be anterior, posterior, anterior and posterior (in case of uterus or cervix in situ), or total (in case of a prolapsed vaginal vault).

Concomitant native tissue repairs were allowed for other less prolapsed compartments or compartments that were not at increased risk of recurrence. To reduce the risk of mesh exposure, simultaneous hysterectomy or T-incisions were avoided.[18] For most of the participating centers it was policy not to simultaneously insert a mid urethral sling because of anticipated increased risk on postoperative urinary retention.[19] Patients were counseled on this strategy and the possibility of a second procedure. In case the presence of stress urinary incontinence post-surgery necessitated the insertion of a mid urethral sling, this was *not* considered a re-intervention for POP and thus not registered as failure; on the other hand the symptomatic recurrence of POP that necessitated re-surgery was a re-intervention for POP and thus counted as a failure.

All procedures were performed under peri-operative antibiotic prophylaxis. Patients received an indwelling catheter for 1to 2 days and a vaginal gauze pack for 24 hours.

Postoperative urinary retention was defined as repeated post-void residual volume > 100 mls measured with a bladder scanner. De novo stress urinary incontinence was considered significant if a patient responded yes; 'moderately to quite a bit' to the question: 'do you experience urinary leakage during physical activity, coughing or sneezing?'

The mesh used in the original trocar-guided Mesh procedure is monofilament polypropylene mesh, weighing 45 gr/m^2. In 2009 some centers started using a partially absorbable mesh, consisting of a fifty-fifty blend of monofilament non-absorbable polypropylene and absorbable polyglecaprone 25 (Prolift+M, Ethicon). The technique is identical, but the mesh weighs 57 gr/m^2 before absorption and after full absorption after 90-120 days only 31 gr/m^2.[20]

Baseline evaluation included medical history and assessment of POP by using the Pelvic organ Prolapse Quantification (POP-Q) System.[11] Data on symptoms and bother were obtained by the standard Dutch urogynecological questionnaire, which among others contains the Dutch validated version of the Urogenital Distress Inventory (UDI).[21]

Follow-up visits were scheduled at 6 weeks, 6 and 12 months. At 12 months a POP-Q examination was performed and patients were again requested to complete the standard urogynecological questionnaire.

Failure outcomes were defined as follows:

- NIH failure mesh treated compartment; POP stage $\geq$ II of mesh treated vaginal compartment(s) or re-surgery for POP in mesh treated compartments within 12 months.
- NIH failure overall POP; leading edge of prolapse in any compartment stage $\geq$ II or re-surgery for POP in any compartment within 12 months.
- Composite outcome failure; leading edge of any compartment > hymen *and* presence of bulge symptoms *or* re-surgery for POP within 12 months.[12]

'Presence of bulge symptoms' was defined clinically significant if a patient responded yes; 'moderately to quite a bit' to either of two questions: 'do you see or do you feel a vaginal bulge?'[21]

To determine the minimum sample size we anticipated on a 90% success rate for the mesh treated compartments.[8, 22, 23] We considered treatment successful if the one-sided 95% confidence interval (CI) did not fall below 85%. This resulted in a minimum number of 282 patients that were necessary for inclusion in this study.

Results are summarized as numbers with corresponding percentages or as medians with range. Primary outcomes were failure percentages with 95% confidence intervals per pre-defined outcome definition. Univariable logistic regression was used to identify possible risk factors of failure in each of the outcomes. Considered risk factors were patient's age, menopause, previous POP repair(s), parity, pre-operative POP stage, Body Mass Index, location of mesh insertion, the use of the new partially absorbable mesh, mesh combined with native tissue repairs, mesh combined with sacrospinous fixation, the presence of the uterus, operating time, blood loss, complications and mesh exposure.

Crude Odds ratios (OR) for the possible risk factors of failure for each outcome were calculated with corresponding 90% confidence intervals (CI). To optimize the validity of the logistic model, restriction of the number of test variables was necessary.[24] To ensure that the number of events per variable (EPV) did not drop below 10, only the allowed number of the most significant variables was selected for entry in the multivariable model. Multivariable logistic regression with forward selection was used to identify those variables that were independently related to failure in each of the outcomes. Variables reaching statistical significance at the $P<0.10$ level in the univariable analysis were considered valid for entry in the forward selection model. The adjusted OR with 95% CI are presented. A P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS 18.0 for Windows.

RESULTS

Four hundred and thirty-three women met the inclusion criteria for trocar-guided mesh surgery and were included. Four hundred and nineteen (97%) completed the 12-month follow up. Baseline characteristics and preoperative POP stage are presented in table 1. Median age of patients was 64 (range 16-93). Seventy-two percent of patients had a recurrent POP and 67% a POP stage ≥ Stage III.

Table 2 shows peri- and postoperative data. Eighteen percent of patients (77) underwent surgery with a partially absorbable mesh. According to the 12-month follow-up questionnaire 38 of 280 (13.6%) patients were classified having de novo stress urinary incontinence.

Table 3 shows failure rates per location of mesh insertion for all pre-defined outcomes. NIH failure of the mesh treated compartments POP stage ≥ II was 15% (95% CI 12-19). NIH failure overall POP stage ≥ II was 41% (95% CI 36-45) and composite failure was 9% (95% CI 7-13). Re-surgery was performed in 18 of 433 (4%) patients, of which sixteen (89%) in the untreated vaginal compartments. Highest failure rates were observed for combined anterior/posterior mesh insertions.

Table 1. Baseline characteristics.

	Total	N (%) or median (range)
Age, years	433	64 (16-93)
BMI, kg/m^2	320	25.6 (18.9-41.8)
Menopause	396	348 (88)
Parity (number)	367	2 (0-7)
Previous POP repair	425	307 (72)
Pelvic organ prolapse		
Stage 0	429	0 (0)
Stage I	429	0 (0)
Stage II	429	141 (33)
Stage III	429	266 (62)
Stage IV	429	22 (5)

POP = pelvic organ prolapse.

Table 2. Peri- and post-operative data.

	Total	N (%) or median (range)
Location tension-free vaginal mesh		
Anterior	433	116 (27)
Posterior	433	152 (35)
Anterior and posterior	433	64 (15)
Total	433	100 (23)
Partially absorbable mesh	433	77 (18)
Mesh procedure combined with native tissue POP repair ('Mesh combined')	432	83 (19)
Sacrospinous ligament fixation	432	26 (6)
Modified Manchester procedure	432	3 (1)
Anterior colporrhaphy	432	17 (4)
Posterior colporrhaphy	432	18 (4)
Perineal repair	432	9 (2)
Enterocele repair	432	10 (2)
Mid-urethral sling	432	5 (1)
Operating time (min)	417	60 (20-150)
Blood loss (ml)	412	100 (0-1300)
Complications*		
Rectal serosa lesion	423	2 (0)
Bladder injury	423	10 (2)
Urinary retention	423	34 (8)
Blood loss > 500 ml	412	4 (1)
Postoperative hematoma	432	22 (5)
Any complication	432	66 (15)
Mesh exposure within 12 months	425	54 (13)

POP = pelvic organ prolapse. * Multiple diagnoses possible.

Table 4 shows crude Odds ratios with 90% confidence intervals per outcome definition for each of the tested variables. Variables that reached statistical significance at the P<0.10 level (shown in bold) were considered valid for entry in the multivariable logistic regression model. Since outcome I resulted in just 64 failures, we only selected 7 of the 9 most significant variables for entry in the multivariable regression model.[24]

Table 5 shows adjusted Odds ratios after multivariable logistic regression analysis. For NIH outcome II (overall POP ≥ stage II), stage of prolapse ≥ III and a solitary mesh, be it anterior or posterior, significantly increased the risk of failure. A combined anterior/posterior mesh with the uterus in situ appeared to be independently associated to failure in all outcomes. Of 35 patients that were diagnosed with a composite outcome failure, 9 had undergone a combined anterior/posterior mesh insertion. Seven of these 9 (78%) patients had a symptomatic descent of the cervix/uterus at 12-months; 4 were operated before the 12-months and underwent vaginal hysterectomy with a McCall procedure, and one an abdominal sacrocolpopexy. One patient was operated beyond the one-year follow-up, but had point C diagnosed at +5 cm at 12-months.

The use of the partially absorbable mesh appeared only to be independently related to NIH failure of the treated compartment.

Table 3. Failure outcomes at 12 months.

	Total	N	Percentage	95% CI
I. NIH failure of mesh treated compartment POP stage ≥ II or re-surgery	415	64	**15**	**(12-19)**
Anterior mesh only	112	20	18	(11-26)
Posterior mesh only	146	9	6	(3-11)
Anterior and posterior mesh	62	21	34	(22-47)
Total mesh	94	14	15	(8-24)
II. NIH failure: overall POP stage ≥ II or re-surgery	419	170	**41**	**(36-45)**
Anterior mesh only	113	60	53	(43-63)
Posterior mesh only	148	66	45	(36-53)
Anterior and posterior mesh	62	30	48	(36-61)
Total mesh	94	14	15	(8-24)
III. Composite failure: overall POP > hymen and bulge symptoms or re-surgery	380	35	**9**	**(7-13)**
Anterior mesh only	106	11	10	(5-18)
Posterior mesh only	127	13	10	(6-17)
Anterior and posterior mesh	58	9	16	(7-27)
Total mesh	87	2	2	(0-8)
Re-surgery	433	18	4	(2-6)
Mesh treated compartment	18	2	11	(1-35)
Untreated compartment	18	16	89	(65-99)
Vaginal bulge symptoms	370	43	12	(9-15)

Data in **bold** are overall percentages with 95% CI per predefined outcome variable.

Table 4. Crude Odds ratios for the risk of failure for all outcomes, using univariable logistic regression analysis.

	NIH treated compartment (I)		NIH overall POP (II)		Composite outcome (III)	
	N	OR (90% CI)	N	OR (90% CI)	N	OR (90% CI)
Age (years)	415	1.01 (0.99-1.03)	419	1.01 (0.99-1.02)	380	0.99 (0.96-1.01)
Menopause (p)	378	0.73 (0.31-1.71)	382	0.69 (0.35-1.34)	346	0.43 (0.16-1.14)
Previous POP repair (p)	407	0.71 (0.44-1.15)	410	0.92 (0.64-1.33)	371	0.97 (0.51-1.86)
Parity (number)	352	1.02 (0.82-1.26)	355	1.01 (0.86-1.18)	326	0.93 (0.70-1.23)
Pre-operative POP-stage	411		415		376	
Stage II		1.00 (reference)		1.00 (reference)		1.00 (reference)
≥ Stage III		**2.35 (1.35-4.11)**		**1.50 (1.05-2.14)**		1.13 (0.59-2.15)
Body Mass Index (kg/m^2)	408	**1.01 (1.00-1.02)**	412	1.01 (0.99-1.02)	376	1.01 (0.99-1.01)
*Location Mesh**	414		417		378	
Total		1.00 (reference)		1.00 (reference)		1.00 (reference)
Anterior		1.24 (0.66-2.32)		**6.47 (3.66-11.42)**		**4.92 (1.36-17.84)**
Posterior		**0.38 (0.18-0.79)**		**4.60 (2.66-7.96)**		**4.85 (1.36-17.28)**
Anterior + posterior		**2.93 (1.53-5.60)**		**5.36 (2.84-10.10)**		**7.81 (2.09-29.20)**
Partially absorbable mesh (p)	415	**3.08 (1.87-5.08)**	418	1.49 (0.98-2.28)	366	1.24 (0.59-2.58)
Mesh combined (p)	414	1.06 (0.61-1.85)	417	0.88 (0.58-1.33)	378	1.05 (0.51-2.18)
Mesh combined with SSF (p)	410	**2.16 (1.00-4.64)**	413	0.63 (0.31-1.29)	363	0.41 (0.07-2.24)
Uterus in situ (p)	417	**2.17 (1.38-3.42)**	417	**2.13 (1.50-3.02)**	366	1.61 (0.89-2.94)
Operating time (per 20 min)	400	**1.01 (1.00-1.02)**	402	0.99 (0.99-1.00)	364	1.00 (0.99-1.01)
Blood loss (per 100 ml)	396	1.00 (0.99-1.00)	398	**0.99 (0.99-1.00)**	360	0.99 (0.99-1.00)
Any complication (p)	414	0.77 (0.33-1.49)	417	0.81 (0.51-1.29)	378	0.30 (0.09-1.01)
Bladder injury (p)	405	0.63 (0.11-3.64)	408	**3.51 (1.11-11.05)**	370	1.20 (0.21-7.06)
Post operative hematoma (p)	414	0.53 (0.15-1.84)	417	1.01 (0.48-2.09)	378	0.50 (0.09-2.78)
Mesh exposure (p)	409	0.85 (0.42-1.74)	413	**0.55 (0.32-0.93)**	372	1.14 (0.49-2.64)

* Total mesh for post hysterectomy vaginal vault prolapse, anterior + posterior mesh for prolapse of anterior and posterior compartments with the uterus in situ.
OR= Odds Ratio. CI= Confidence Interval. (p) = Absent coded as 0, present coded as 1.POP= pelvic organ prolapse.
Bold numbers: Variables reaching statistical significance at the p<0.10 level, valid for entry in the selection procedure.

Table 5. Adjusted Odds ratio for the risk of failure for all outcomes, using multivariable logistic regression analysis.

	NIH treated compartment (I)		NIH overall POP (II)		Composite outcome (III)	
	N	**OR (95% CI)**	**N**	**OR (95% CI)**	**N**	**OR (95% CI)**
Pre-operative POP-stage	402		378			
Stage II		NS (p=0.65)		1.00 (reference)		-
≥ Stage III		NS (p=0.65)		**2.30 (1.36-3.89)**		-
Body Mass Index (kg/m^2)	402	1.01(0.99-1.02)		-		-
*Location Mesh**	402		378		378	
Total		1.00 (reference)		1.00 (reference)		1.00 (reference)
Anterior		0.87 (0.40-1.92)		**7.70 (3.70-16.03)**		4.92 (1.06-22.84)
Posterior		**0.36 (0.15-0.88)**		**7.66 (3.61-16.25)**		**4.85 (1.07-22.05)**
Anterior + posterior		**2.65 (1.21-5.81)**		**5.40 (2.38-12.21)**		**7.81 (1.62-37.60)**
Partially absorbable Mesh (p)	402	**2.46 (1.27-4.77)**		-		-
Uterus in situ (p)	402	NS (p=0.61)	378	NS (p=0.44)		-
Blood loss (per 100 ml)		-	378	NS (p=0.27)		-
Bladder injury (p)		-	378	2.59 (0.59-11.33)		-
Exposure (p)		-	378	NS (p=0.22)		-

* Total mesh for post hysterectomy vaginal vault prolapse, anterior + posterior mesh for prolapse of anterior and posterior compartments with the uterus in situ.
NS: not selected. **Bold** values are statistically significant at p<0.05.

COMMENT

Failure rates are highly dependent on outcome definition. The composite outcome showed the lowest failure rate, but appeared not to be significantly different from the NIH outcome of the mesh treated compartments (9%, 95% CI 7-13 vs. 15%, 95% CI 12-19). With 41% (95% CI 36-45) the NIH outcome II (leading edge of any prolapsed compartment stage ≥ II) showed the highest failure rate. Stage of prolapse ≥ III was predictive for failure in NIH outcome II. Predictor of failure for all of the outcomes was the location of mesh insertion. Particularly a combined anterior/posterior mesh with the uterus or cervix in situ increased the risk of failure in all outcomes.

One of the weaknesses of this study is that an examiner at the 12-month follow--up was not blinded. Use of unblinded POP-Q staging might underestimate overall recurrences.[25] Another drawback is the relatively short follow-up period of 12 months. Strengths on the other hand were the use of validated tools of measurement, such as POP-Q and validated questionnaires to objectify symptoms and bother.[11, 21] Further strengths are the study's prospective data registry and large sample size.

This study clearly demonstrates the importance of the outcome definition when reporting results of POP surgery. Although it seems logical to focus on the outcome in mesh treated vaginal compartment(s), this blurs overall anatomic outcomes as is demonstrated and by others.[12, 26] Focusing on anatomic criteria only, easily verifiable to the physician, does ignore a patient's perception of symptoms, for which she primarily had sought relief. Chmielewski et al have reanalyzed data of a randomized trial of three techniques of anterior colporrhaphy and revealed considerably better success with the use of this clinically relevant composite outcome compared with strict anatomic criteria.[26] These authors also stated that there is a considerable portion of women who receive routine gynecologic care that have a POP stage II on straining and would therefore not meet the NIH Workshop criteria of a 'satisfactory' treatment result.[10, 27, 28] This is comparable with data from a large Dutch cross sectional study among community dwelling women, that revealed that of women aged between 45 and 85 years, 36,5% were diagnosed with a stage I and 33% with a stage II prolapse, of whom only 6,9% of women with stage I and 15,8% of those with stage II experienced vaginal bulge symptoms as opposed to 43,3% of women with stage III and 100% of those with stage IV prolapse.[29] A large proportion of women with stage II prolapse is thus asymptomatic and should be considered to have 'physiological' pelvic organ support. We therefore strongly agree with Barber et al that their suggested composite outcome of success, whereby the hymen is regarded as threshold for anatomic success and the absence of bulge symptoms as patients reported sign of symptom relief, is the most realistic outcome for prolapse surgery and should be the outcome of choice in future studies.[12] In this analysis we have used a composite *failure* outcome. Since we were particularly interested in patients with prolapse beyond the hymen that was symptomatic, the inclusion of bulge symptoms in our definition of composite failure was obligatory.

The large difference in outcome of the mesh treated compartments and overall POP, seems to be due to the effect that the treatment of only one vaginal compartment can have on the remaining non-treated compartments as was demonstrated in earlier

work of us and other studies.[12, 14, 26] This finding is emphasized by the overall re--surgery rate of 4% (18 out of 433 patients), of which only 11% (2 out of 18 patients) were re-interventions in the mesh treated vaginal compartment, but the vast majority of 89% (16 out of 18 patients) in the non-treated vaginal compartments. These results are comparable with data of a recently published retrospective French study on 524 patients, of whom 3% underwent repeat surgery for prolapse recurrence, in particular of the untreated vaginal compartments.[30] The odds ratios for overall failure stage ≥ II after solitary mesh insertions were high and significant (table 5). In an earlier study on 150 mesh treated patients we demonstrated that 46% of patients after solitary anterior mesh, and 25% after solitary posterior mesh insertion developed de novo prolapse stage II or more in the previously unaffected vaginal compartments.[14] It was recently demonstrated that mesh insertion compared with a native tissue repair of only one vaginal compartment is responsible for a greater risk of de novo prolapse in other untreated vaginal compartments.[31] This secondary analysis of a randomized controlled trial, that compared mesh with native tissue repair in patients with recurrent prolapse, revealed that 47% of women that underwent mesh insertion in only one vaginal compartment developed a *de novo* prolapse in untreated vaginal compartments, compared to only 17% of women after native tissue repair of only one vaginal compartment. These data indicate that we have to reconsider our surgical strategies when using mesh in only one vaginal compartment.

In contrast with a solitary posterior mesh, a solitary anterior mesh was no risk factor for failure in the composite outcome. Apical suspension is considered crucial in prolapse surgery.[32] A solitary posterior mesh has the advantage of additional apical support by its bilateral sacrospinous suspension. It is well known that sacrospinous ligament fixation facilitates anterior vaginal walls to descent.[33] We hypothesize, that a solitary posterior mesh, by its strong reduction of prolapse enhances the effect that sacrospinous ligament fixations already have on the anterior vaginal wall. This may contribute to a greater and consequently symptomatic descent of the anterior vaginal wall.

The combination of an anterior/posterior mesh with the uterus or cervix in situ appeared independently associated to failure in all outcomes. Multivariable regression analysis clearly showed that it was not the single fact of the uterus being in situ, but the combination of an anterior/posterior mesh with the presence of the uterus that appeared independently associated to failure. Alternative treatment for this simultaneous mesh insertion and fixation to the uterus could be a single anterior mesh combined with a sacrospinous hysteropexy. Concomitant midline fascial plication of the posterior vaginal will adequately treat any prolapsed posterior compartment, if necessary.[9, 34] This strategy offers the advantage of reduced mesh usage, particularly since the evidence for the use of mesh in the posterior compartment is still limited.[1] Another approach to the combined anterior/posterior mesh insertion with pronounced uterine descent would be supracervical laparoscopic sacrocolpopexy.[35]

The use of the partially absorbable mesh was only independently related to failure in the NIH treated compartment outcome, but to none of the others. The use of this lighter weight mesh has potential advantages over the heavier-weight original mesh

and might be responsible for lesser mesh contraction, less pelvic pain and de novo dyspareunia.[20] However, the evidence that the use of this partially absorbable mesh is superior to native tissue repair surgery still has to be delivered by well-designed controlled clinical trials.

Complication rates in this cohort were comparable with other large studies using this mesh.[4, 36, 37] Mesh exposure rate in this series was 13%. It has recently been reported that most of these mesh exposures are asymptomatic and that two thirds of these resolve after minor surgery. It has also been demonstrated that the experience of the surgeon has a protective effect on the risk of mesh exposure.[38]

Recently a FDA Public Health Notification update informed the public in the United States on the potential serious complications of trans-vaginal mesh surgery and gave recommendations, among which, proper training of the surgeon was one.[39] We therefore believe that only experienced surgeons who are capable of treating an adequate volume of patients should be allowed to perform this vaginal mesh surgery. The finding that experience of the surgeon diminishes the risk of complications supports this statement.[30, 38] Future research should focus on surgeons' experience as a potential risk factor for failure; this might give insight into the learning curve aspects of vaginal mesh surgery.

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8

GENERAL DISCUSSION AND FUTURE PERSPECTIVES

GENERAL DISCUSSION

More than fifteen years have passed since the publication of the 'Olsen' paper.[1] The challenges to science as stated in the introduction of this thesis have been honoured, but have we achieved our goals and optimized the outcomes of vaginal prolapse repair surgery?

This section of the thesis is a reflection of the response to these challenges and to the research questions in the outline of this thesis.

The first challenge was to reduce recurrence rates and increase the durability of POP repairs. We believe that we certainly have contributed to this aspiration, but have not entirely been able to prove this in the work presented in this thesis. The first reason for this is that most of the studies that were performed and presented in this thesis were observational by nature, and since most of them lacked a control group, it is difficult, if not impossible, to determine their acclaimed superiority over other traditional type of POP repairs. The second reason is that follow up periods of one year are fairly short to claim increased durability of a repair. Longer follow-up periods are absolutely mandatory as are well-designed randomized controlled trials to definitely determine the position of new vaginal POP repair procedures.

The second challenge was to optimize and standardize the assessment of patients' symptomatology and anatomical and functional outcomes of POP repairs. We honestly believe that this goal has been achieved, as is demonstrated by the results presented in the studies of this thesis. The studies presented here, have been performed with pre- and postoperative anatomic and functional assessments by the systematic use of POP-Q and validated Health related Quality of Life Questionnaires and Sexual Function Questionnaires. These have enabled us to clearly and accurately objectify both anatomical and functional outcomes, that are indispensable for the comparison with other surgical treatments of POP that have used the same tools of measurement. Therefore it is absolutely necessary to internationally agree on which tools of measurement have to be used. The use of POP-Q has definitely shown its indispensable value in anatomical outcome assessment.[2, 3] And for the criticasters of POP-Q, who state it is to difficult or time consuming to perform a POP-Q, Karp et al have recently shown that among examiners who routinely perform POP-Q examinations, there is no significant difference between "eyeball" estimated and measured POP-Q values and stage.[4]

The systematic use of the standard Dutch Urogynecological questionnaire in all of the presented studies has greatly contributed to insight in the effect of surgery on patient symptomatology and its relation to pelvic floor disorders. This is particularly the achievement of van der Vaart et al who validated the Dutch version of the UDI, and a few enthusiastic 'Wergroep Bekkenbodem' members who selected and compiled all items that are present in the latest version of 2006 (see questionnaires in appendices).[5-8] Although the Defecatory Distress Inventory (DDI) has been used in numerous Dutch studies and has proven its value, an official Dutch validation of the DDI has not yet been published.[9, 10] For that reason and in order to join up internationally, we now feel it to be the right time to validate the Dutch versions of the PFDI-20 and PFIQ-7 for the purpose of international comparison of functional

outcomes of studies.[11] This may also particularly facilitate the Dutch participation in international studies.

The Dutch validated version of the PISQ-12 has shown its advantages in these respects already.[12] However, the present PISQ-12 might not be sensitive or condition--specific enough to be able to discriminate in aspects of sexual function, and therefore it would also be of value to participate in the Dutch validation process of the translated revised PISQ, the 'PISQ-R'. This process is under the supervision of the International Urogynecological Society.

Although the use of changes in the various domains scores of the UDI, DDI and IIQ have shown their value in the assessment of functional outcomes, we do believe that the addition of calculated effect sizes in particular domains might greatly contribute to the clinical relevance of statistically significant changes, and thus facilitates clinical interpretation of functional results.[13]

However, quantization of anatomy is important as is that of function and patients symptomatology, but data from the Dutch Brielle study have clearly demonstrated that prevalence of feeling and/or seeing a vaginal bulge in all women aged 45 to 85 years was only 12.1%, while 38.5% of examined women were diagnosed with a POP stage II or more.[14] This discrepancy clearly demonstrates that not all women with a POP stage II are bothered by vaginal bulge symptoms, and might be considered to have physiological pelvic organ support. This discrepancy also underlines the importance of choosing the right outcome measure in surgical POP studies. Most of the studies presented in this thesis have used the internationally accepted NIH outcome measures, which actually aim at what at present could be considered more or less 'supra-physiological' anatomic outcomes (stage 0 and I), and as a consequence are more a representation of so called 'doctors' goals', in stead of being a reflection of the relieve of a patient's bother and complaints caused by POP.[15, 16] The NIH criteria are very strict and, with the present scientific knowledge, seem of limited value, since Barber et al have demonstrated that the postoperative absence of vaginal bulge symptoms had the most significant relationship with a patient's assessment of overall improvement, while strict anatomic success alone did not.[17] These authors therefore suggested to use a composite outcome that includes the absence of bulge symptoms in addition to anatomic criteria and the absence of re-treatment. They agreed with Swift et al to use the hymen as the threshold for anatomic success.[18] We strongly agree with these authors that this newly proposed composite outcome, which is a combination of more realistic anatomic outcome criteria (leading edge of prolapse < hymen) with the most specific prolapse symptom of seeing and/or feeling of a vaginal bulge, to be the best and most realistic outcome measure. We therefore suggest this composite outcome to be the outcome of choice in future studies on the surgical treatment of pelvic organ prolapse.

We have also shown in this thesis that the composite outcome failure in a large cohort of mesh treated patients did not significantly differ from the anatomic outcome failure rate of the treated compartment only, but was very significantly different from failure in overall POP outcome according strict NIH criteria. This finding also underlines the statement that in future studies, and particularly in randomized controlled trials

that compare two surgical POP procedures, the composite outcome should be used as the primary outcome measure, since it is the best reflection of patient's reported outcomes. Since all anatomical and functional data presented in this thesis have been collected in a standardized manner and are stored in the Radboud University database, it is very well possible to perform re-assessments of the outcomes of the studies performed, using this new composite outcome measure.[17]

Re-assessment of important randomized controlled trials that so far demonstrated significant anatomical benefits for one procedure, in this case vaginal mesh insertion, could come to different conclusions when using this new outcome measure, since most of these studies could not demonstrate a significantly superior functional outcome.[19-21] One important trial already showed very different outcomes after re--assessing the original data with the new composite outcome measure.[22, 23]

Part of the composite outcome is the presence of a re-intervention. But what do we consider is a relevant re-intervention? Re-surgery in the prolapse-treated compartment is an obvious re-intervention that will not be prone to any discussion, but what about de novo prolapse in an untreated and previously well supported vaginal compartment, or urinary stress incontinence that appeared occult prior to surgery, but is unmasked postoperatively as a consequence of appropriate reduction of one of the prolapsed vaginal compartments.[24, 25] It is necessary therefore, when using the proposed composite outcome, to predefine clearly what is considered a re-intervention after prolapse surgery as well.

So which aspects of scientific insight have been optimized?

In chapter 2 we have shown that midline fascial plication for posterior vaginal wall prolapse is an effective anatomic treatment with considerable symptom relief as shown by improvements in UDI, DDI and IIQ domain scores. Two third of patients that suffered from obstructed defecation experienced relief of bother or cure after the procedure. The effect size of symptom relief was large (1.5). We also learned that predictors of anatomic failure of this procedure were a posterior vaginal wall prolapse stage ≥ III and a prior colposuspension. In these cases one might consider to treat patients with a trocar-guided mesh insertion of the posterior vaginal wall.

The augmentation of traditional colporrhaphies with a synthetic Titanium coated mesh has not resulted in better anatomic outcomes when compared with plain native tissue colporrhaphies without augmentation at the short-term follow-up (chapter 3). Although the observational cohort study presented in this thesis lacked a control group, POP-Q comparison with historical research articles supports that conclusion. The tension-free vaginal mesh insertion between bladder and vagina and/or bowel and vagina is a revolutionary and more causal way of treating the hernia that occurs with POP.

Although results of the total Prolift™ procedure for post hysterectomy vaginal vault prolapse showed excellent anatomic results, as shown in chapter 4, these have to be counterbalanced against potential adverse effects, such as mesh exposure, pain and dyspareunia, not only at the one-year follow up, but at longer term evaluation as well. Although the functional results showed favorable outcomes in our two center experience of this paper as well, scientific evidence of superiority can only be obtained

by well-designed randomized controlled clinical trials, comparing this procedure with the established golden standard procedure, the laparoscopic sacral colpopexy.[26] Both procedures have comparable and considerable learning curves and it hardly ever happens that one surgeon is equally experienced in both procedures, so fair comparison remains troublesome.[27] It has been shown that every decade of clinical experience significantly reduces the risk of complications in vaginal mesh surgery.[28] Therefore results of such controlled trials will be influenced and are hampered by the experience of the surgeon in either of these techniques.

In chapter 5 we could demonstrate the low rate of de novo dyspareunia and absence of clinically relevant shrinkage of the partially absorbable polypropylene mesh in Prolift+M, which is an encouraging improvement in the development of mesh-reinforced surgery.

In chapter 6 we could demonstrate that mesh exposure, a fairly frequent complication of vaginal mesh surgery, has been found to be independently associated with deterioration in sexual function. Although we could not detect a difference in mean sexual function scores, measured with the PISQ-12 at 12 months, we did observe that sexual function was affected differently by either trocar-guided mesh insertion or by native tissue repair. Improvement in the sexual function scores of the native tissue arm was entirely attributed to improvements in the physical and partner related subscales, while in contrast with this, slight improvements in the physical subscale in the mesh arm were nullified by deteriorations in the behavioral/emotive subscale. The fibrotic reactions to the vagina caused by the mesh could possibly be responsible for a hampered physiological response of the vagina to sexual stimuli. Furthermore there could be a difference in perceived body image by women, but also by their spouses, between mesh insertions and native tissue repairs.[29, 30] Male sexual function following prolapse repair of their sexual partners needs to be more thoroughly examined in the future as well.

We have demonstrated in chapter 7 that outcome of prolapse surgery in trocar--guided tension free vaginal mesh insertion clearly depends on outcome definition. Conventional (NIH) mesh treated and newly suggested composite outcomes did not differ at one year. We could however demonstrate that a combined anterior/posterior vaginal mesh insertion with the uterus in situ is a risk factor for failure in all of the predefined outcomes.

CONCLUDING ANSWERS TO THE RESEARCH QUESTIONS

- Anatomic and functional outcomes of midline fascial plication under continuous digital transrectal control for posterior compartment prolapse were good. Overall anatomic success was 80% (95% CI 75-86). Risk factors for anatomic failure were initial size of posterior vaginal wall prolapse (stage ≥ III) and prior colposuspension.
- Ultra lightweight titanized polypropylene mesh to augment conventional prolapse repair surgery showed minimal morbidity, but no additional value compared to conventional surgery at short-term follow-up.

- Trocar-guided total tension-free vaginal mesh (Prolift™) repair with one continuous piece of mesh for post-hysterectomy vaginal vault prolapse is well tolerated and anatomically and functionally highly effective. Anatomic success was 91% (95% CI 83-99). Mesh exposure rate was 15%.
- The use of a partially absorbable mesh in trocar-guided mesh repair of POP stage ≥ III showed improved anatomic support at one-year, with excellent functional improvements, without apparent safety concerns. Rate of the novo dyspareunia was 2% at one-year follow-up. Sexual function scores, measured with the PISQ-12 increased significantly post-surgery.
- Sexual function scores, measured with the PISQ-12 were not different at one-year in patients with recurrent prolapse who were surgically treated with either a trocar-guided mesh insertion or by vaginal native tissue repair. Mesh exposure appeared independently associated with deterioration in sexual function.
- In a comparison of outcomes of a large cohort of trocar-guided vaginal mesh surgery conventional mesh treated outcome did not differ significantly from a newly suggested composite outcome. Treated compartment outcome failure was 15% (95% CI 12-19), Composite outcome failure was 9% (95% CI 7-13). A combined anterior/posterior mesh insertion with the uterus in situ appeared to be a risk factor for failure in all outcomes.

GENERAL CONCLUSION

In conclusion one can say that good research starts with well-designed observational cohort studies with proper anatomic and functional outcome measures. The composite outcome with adjusted anatomic criteria (leading edge of prolapse < hymen) with the postoperative absence of vaginal bulge symptoms and the absence of *prolapse* retreatment should be the outcome of choice. The results of these observational studies can subsequently be used for the power calculations that are necessary for the search of the supremacy of one of either technique in a Randomized Controlled Trial. Although we admit that well designed randomized controlled trials are necessary, we believe and we have demonstrated that well designed prospective cohort studies with considerable sample size can offer us very valuable information, particularly on certain risk factors, and are not necessarily considered an inferior clinical research tool.

HOW ABOUT THE FUTURE?

Future research, with regard to the perspective of this thesis, should focus on the validation of the internationally used PFDI-20 and PFIQ-7 and PISQ-R. The impact of body image on sexual function following POP surgery, as well as the impact of this surgery on male sexual function deserves further research. In a broader perspective, and considering the sharp rise in the aging population, further research should focus on the development of a durable, safe and patient friendly solution to pelvic organ prolapse in general. Longer-term observation of mesh treated patients is absolutely

mandatory, but in the mean time further improvements in the biocompatibility of synthetic meshes are warranted. One might also think of protective coatings on meshes, such as silver to prevent infection, or for example partially, or delayed absorbable meshes that serve as scaffolds and are pre-seeded with (stem?) cells to improve collagen quality and improve durability of prolapse repairs without the potential negative side effects of mesh contraction for example.[31, 32]

Another important subject of research should focus on the prevention of pelvic organ prolapse, and more in particular on research of the molecular and biochemical genetic basis of pelvic organ prolapse, so that our understanding of genetic predispositions may expand and possibly and hopefully will provide us in the future with means and tools to modify these genetic predispositions in one way or another.[33] With the expected epidemic of pelvic organ prolapse to come, as a result of the aging population, there will be and will remain enough challenging topics for basic and clinical research of pelvic organ prolapse.

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9

SUMMARY & SAMENVATTING

SUMMARY

This thesis is about optimizing outcomes of vaginal prolapse surgery with and without mesh.

Chapter 1 provides a general introduction on the subject of pelvic organ prolapse (POP). The definition, history, prevalence, aetiology and riskfactors, pathophysiology, clinical presentation and management of POP are being discussed. The second part of the general introduction focuses on the 'Why-Question' of this thesis. The two challenges that were the inspiration of this thesis are being discussed.

The first challenge was: is it possible to reduce recurrence rates and increase durability of POP repairs. The second challenge was: is it possible to optimize assessment of symtomatology and anatomical and functional outcomes of POP repairs?

After a brief description of the trocar-guided tension-free vaginal mesh technique and an explanation of the use of the POP-Q system and Symptom Bother and Health related Quality of Life questionnaires, the main research questions are formulated in the outline of this thesis.

Chapter 2 provides the detailed description of the surgical procedure and the anatomical and functional results of the midline fascial plication under continuous digital transrectal control of 233 patients with a posterior vaginal wall prolapse stage ≥ II. Posterior colporrhaphy is one of the most commonly performed gynecological procedures in over 40% of women undergoing surgical correction of pelvic organ prolapse. The described surgical procedure is actually a hybrid of the *defect discrete repair* that was 'en vogue' in the nineteen nineties of the last century and the *classical* midline plication of the posterior vaginal wall. The addition of the digital transrectal control is thought to aid in identifying 'fascial' defects and in checking whether the repair is 'solid' enough.

The anatomic success rate, according strict NIH criteria (POP stage < II), was 80.3% (95% CI 75-86).

Functional results were good as shown by the decrease in patient bother as expressed by various significant improvements in mean domain scores of the UDI, DDI and IIQ. Effect sizes were calculated as well, with the intention to further objectify the clinical relevance of statistically significant findings. Large effect sizes were demonstrated for the domain of genital prolapse and pain of the UDI in particular, and for the domains of physical functioning and mobility of the IIQ. Only 25% of patients were bothered by obstructed defecation, while 75% were not. Sixty-three percent of patients, that were significantly bothered by obstructed defaecation, experienced cure or relief from their symptoms one year post-surgery. In that subgroup of patients the effect size of surgery on obstructed defecation symptoms was particularly high (effect size: 1.5).

Logistic regression analysis identified two independent predictors of anatomic failure: a posterior vaginal wall prolapse stage ≥ III and a prior colposuspension.

Chapter 3 provides a detailed description of the surgical technique and anatomical and functional outcomes of 71 patients who underwent vaginal prolapse repair surgery augmented by ultra lightweight titanium coated polypropylene mesh. In contrast with the tension-free vaginal mesh insertion, this technique merely aims

to augment traditional vaginal colporrhaphies. No full thickness incision was made, but a cleavage of the vaginal wall after hydro dissection and consequently a plication took place of what is called the 'fascial' remnants of the vagina. The mesh, compared to the polypropylene meshes used at that time, was, and still is ultra lightweight (16 gr/m2) and covered with a thin layer of titanium to reduce foreign body reactions that could be the cause of mesh contraction and subsequently pelvic pain.

Outcome measures were conventional NIH criteria; POP stage < II. Anatomic failure in the anterior vaginal compartment was 36%, which is not significantly different from historical anatomic data after anterior vaginal wall repairs. Remarkably, though defined as failures, the prolapse domain scores of these 'failed' patients dropped dramatically from 50 (range 0-100) before surgery to 7 after mesh augmentation. For the posterior vaginal compartment the failure rate was 18%. A weakness of this study was the fairly short follow-up period; comments on the durability of the repair are therefore difficult to make. Furthermore apical restoration was not systematically performed in this patient series, which could be one of the explanations for the relatively high failure rate in the anterior compartment.

Mesh exposure was 5.6 %, which is low if compared to conventional heavier weight polypropylene. Whether augmentation with this type of synthetic mesh could have contributed to the durability of prolapse repairs can only be determined after well designed randomized controlled trials, comparing conventional native tissue repairs and repairs with titanium coated mesh augmentation. The evolution in mesh surgery however, has taken a slightly other direction.

Chapter 4 offers a detailed description of the trocar-guided total tension-free vaginal mesh repair of post-hysterectomy vaginal vault prolapse. Anatomical and functional outcomes of a cohort of 46 patients are presented. This medium weight synthetic mesh (45gr/m2) is inserted by the use of trocars through the obturator foramen for the anterior compartment and bilaterally through the buttocks and sacrospinous ligaments for the posterior compartment, and is inserted underneath the full thickness layer of the vagina. This is in contrast with the augmentation technique described in chapter 3. This total TVM technique uses only one piece of mesh, which simultaneously treats the anterior and posterior vaginal compartments, and by passing under an apical bridge of the vagina does provide apical suspension by the use of both sacrospinous liagaments.

Anatomical outcome, defined as overall POP stage <II was 91% (95% CI 83-99). Mesh exposure occurred in 15% of patients and was slightly higher than the 10% seen in all trocar-guided mesh procedures together at that time, but was mostly asymptomatic. A slight, though statistically significant shortening of the vagina was observed and is probably related to mesh contraction.

De novo dyspareunia rate was 18%, but in 28% of patients pre-existing dyspareunia resolved after surgery. Patients' Global Impression of Improvement was high: 93% of patients experienced the present situation with respect to prolapse to be much or very much better at one-year post-surgery.

Chapter 5 provides one-year anatomic and functional outcomes of trocar-guided mesh repair of vaginal prolapse using a partially absorbable mesh. This observational

cohort study comprised 128 patients and was performed in 11 urogynecological sites across Europe and the United States. The technique of mesh placement was the same as in the original Gynecare Prolift Pelvic Floor repair system, but the mesh was entirely different: partially absorbable and more elastic, particularly in the longitudinal direction. This mesh contains equal parts of monofilament non--absorbable polypropylene and absorbable polyglecaprone 25. Before absorption this mesh weighs approximately 57 gr/m^2 and after full absorption after 90-120 days only 31 gr/m^2.

At one year follow-up anatomic outcome, defined as POP stage < II for the mesh treated compartment, was 77.4 % (95% CI 69-84). Functional outcomes showed significant improvements in all subscales of disease-specific symptoms and Quality of Life scores from baseline to one-year. Sexual function scores, measured with the PISQ-12 increased significantly at one year with an average of 5.2 points.

De novo dyspareunia rate was only 2 %. Eighty-nine percent of patients experienced the result post-surgery to be 'much better' compared to their situation before surgery. There were no apparent safety concerns with this new lighter weight mesh and the absence of clinically relevant shrinkage combined with the low rate of the novo dyspareunia was particularly encouraging.

Chapter 6 provides the results of a study on sexual function in patients with recurrent POP, who were treated surgically by either trocar-guided mesh insertion or vaginal native tissue repair. Sexual function was measured with the PISQ-12 at baseline and at one-year post-surgery. This study was a secondary analysis of study VROUW I, a randomized controlled trial, that primarily aimed to compare anatomic outcomes of the treated vaginal compartments in patient with recurrent POP, who were randomly assigned to either a conventional native tissue repair or tension-free vaginal mesh insertion with the Prolift™ mesh kit. Of the 194 original patients, 78 in the mesh arm and 50 in the native tissue arm were ' sexually active'. A total of 60 patients completed the PISQ-12 both at baseline and at one-year and were included in the present analysis. Fifty-eight patients were labeled as 'incomplete responders' since they only completed the questionnaire at baseline or at one-year.

In this study we could not observe a difference in mean total PISQ-12 scores at one-year between the two treatment arms. However sexual function was affected differently. The native tissue repair arm showed an increase in mean total PISQ-12 score, which could be entirely attributed to significant improvements in the physical and partner related subscales. Total PISQ-12 scores virtually remained unchanged in the mesh group though. Subscale analysis revealed that improvements in the physical subscale were nullified by deteriorations in the behavioral/emotive subscale, which was attributed to significant declines in the frequencies of orgasm and being sexually excited.

The explanation for this difference is sought in the potentially adverse effect that insertion of a synthetic mesh could have on the physiological response of the vagina to sexual stimuli, a possibly altered body image after a prolapse repair with a mesh and/or a different perception that the male partner could have of his sexual partner after a prolapse repair with a mesh.

The presence of a mesh exposure appeared to be independently associated with deterioration of sexual function scores.

Chapter 7 deals with the comparison of different outcome definitions for failure in prolapse surgery. Conventional *NIH Workshop* failure outcomes (pelvic organ prolapse stage ≥ II) were compared with a newer, clinically more relevant, composite failure outcome (pelvic organ prolapse in any compartment beyond the hymen *with* bulge symptoms *or* repeat surgery for pelvic organ prolapse). In this prospective observational cohort of 433 patients treated by trocar-guided vaginal mesh insertion, failure rates varied from 9% (95% CI 7-13) for the composite outcome to 41% (95% CI 36-45) for NIH failure outcome of POP in any vaginal compartment. The composite failure outcome appeared not statistically different from the NIH failure outcome of the mesh treated compartment only (15%, 95% CI 12-19). Since the composite outcome includes patients' bulge symptoms we strongly recommend to use this outcome measure in future studies.

The second objective of this study was to identify independent predictors of failure for these outcomes by means of logistic regression analysis. Independent predictor for failure in all outcomes was the combined anterior/posterior mesh insertion with the uterus in situ.

Chapter 8 is a general discussion on the findings of this thesis and provides the answers to the research questions posed in the outline of this thesis. Furthermore it discusses some challenging aspects of future research that comprehend the aetiology, prevention and future alternative treatments of pelvic organ prolapse.

SAMENVATTING

Dit proefschrift handelt over het optimaliseren van uitkomsten van prolapschirurgie met en zonder het gebruik van mesh.

Hoofdstuk 1 geeft een algemene inleiding over het onderwerp genitale prolaps. De definitie, geschiedenis, prevalentie, etiologie en risicofactoren, pathofysiologie, klinische verschijningsvorm en behandeling van prolaps komen ter sprake. Het tweede deel dan de algemene inleiding richt zich op de *waarom-vraag* van dit proefschrift. De twee uitdagingen die de bron van inspiratie voor dit proefschrift waren worden besproken.

De eerste uitdaging betrof de vraag: is het mogelijk de recidiefkans van prolaps na chirurgische behandelingen te verlagen en de duurzaamheid van de plastieken te verhogen? De tweede uitdaging betrof de vraag of het mogelijk is de symptomatologie van genitale prolaps en de anatomische en functionele uitkomsten meer gestandaardiseerd in kaart te brengen.

Na een korte beschrijving van de introductie van de 'spanningsvrije mesh techniek' en een uitleg over het gebruik van POP-Q en Symptoom- en Kwaliteit van Leven vragenlijsten, worden de belangrijkste onderzoeksvragen van dit proefschrift geformuleerd.

Hoofdstuk 2 geeft een gedetailleerde beschrijving van de chirurgische procedure en de anatomische en functionele uitkomsten van de '*fascie plicatie onder voortdurende digitale transrectale controle* bij 233 patiënten met een achterwandprolaps stadium II of hoger. Een achterwandplastiek is een veelvuldig uitgevoerde prolapsoperatie en is verantwoordelijk voor 40% van het totaal aantal uitgevoerde vaginale prolapsoperaties. De beschreven ingreep is eigenlijk een hybride van het zogenaamde *defectspecifieke* herstel van de achterwand, die in de jaren '90 van de vorige eeuw 'en vogue' was en de *klassieke* plicatie van de fascie van de vagina-achterwand. De toegevoegde *controle met de intra-rectale vinger* vergroot de kans op het herkennen van fasciedefecten en helpt bij het controleren van de stevigheid van de plastiek.

Het anatomische succespercentage van deze behandeling van het achterste compartiment is volgens de strikte NIH criteria (prolaps stadium < II) 80.3% (75-86).

Functionele resultaten waren eveneens zeer bevredigend. Er was een significante reductie in prolapsgerelateerde klachten, te meten in meerdere domeinen van de Plas Klachten Lijst (UKL), de Defaecatie Klachten Lijst (DKL) en in de Kwaliteit van Leven Impact Klachten Lijst (IKL). Klinisch relevante effecten werden waargenomen in de domeinen prolaps en pijn van de UKL en in de domeinen fysiek functioneren en mobiliteit van de Kwaliteit van Leven Impact Lijst.

Slechts 25% van de behandelde patiënten vertoonde preoperatief symptomen van 'faeces evacuatiestoornissen'. Tweederde van deze groep patiënten ervoer verbetering of genezing van hun klachten na chirurgische behandeling.

Met behulp van Logistische regressie konden twee risicofactoren voor anatomisch falen worden geïdentificeerd: 1. een achterwandprolaps stadium III of hoger en 2. een voorafgaande suspensie van de blaashals.

Hoofdstuk 3 beschrijft de chirurgische techniek en de anatomische en functionele resultaten bij 71 patiënten die een versteviging van een conventionele voor en/of achterwandplastiek ondergingen met een ultra lichtgewicht getitaniseerde polypropyleen mat. De gedachte achter de titanium coating is een mogelijk geringere *vreemd-lichaam* reactie en minder littekenvorming en *mat-krimp* met als gevolg minder kans op pijn dan bij het gebruik van zwaarder polypropyleen meshmateriaal dat in die tijd werd gebruikt.

Volgens de voor die tijd gebruikelijke strikte anatomische uitkomstmaten, was het anatomisch 'faal' percentage 36% voor de vagina voorwand. Dit percentage verschilde niet van studies die geen matversteviging gebruikten. Voor het achterste compartiment was het 'faal' percentage 18%; eveneens niet verschillend van gebruik zonder matversteviging. Een zwakte van het onderzoek is de betrekkelijke korte periode tot na controle en het te weinig aandacht schenken aan het belang van middelste compartiment suspensie. Dit kan een van de redenen zijn dat de succes cijfers matig waren. Ondanks het matige anatomische succescijfer, was bij het overgrote deel van de patiënten het verzakkinggevoel postoperatief verdwenen, zich uitend in een zeer lage prolaps domein score van de UKL bij na controle.

Mesh *exposure*, ofwel het 'zichtbaar worden van de mat' in de vagina werd waargenomen bij 5.6 % van de patiënten. Dit percentage is laag vergeleken bij cijfers over het gebruik van conventioneel, zwaarder polypropyleen mesh materiaal. Of de toevoeging van deze getitaniseerde mesh een duurzamer prolaps plastiek resultaat oplevert, kan alleen worden vastgesteld na een goed uitgevoerd gerandomiseerd en gecontroleerd onderzoek.

Hoofdstuk 4 geeft een gedetailleerd beeld van de trocar-geleide totale spanningsvrije mesh behandeling voor vagina-top prolaps na voorafgaande verwijdering van de baarmoeder. Van 46 patiënten die deze behandeling ondergingen en die de jaar controle hadden voltooid worden de anatomische en functionele resultaten beschreven. Bij deze techniek wordt een aansluitend stuk polypropyleen mesh gebruikt dat dient ter ondersteuning van zowel het voorste, het achterste, als het middelste compartiment. Het anatomisch succespercentage was 91 % (83-99). Bij 15% van de patiënten echter werd een meshexposure waargenomen.

Bij 18% werd pijn bij het vrijen gesignaleerd die voor de operatie niet was gerapporteerd. Bij 28% van de patiënten echter, was de pijn die voor de operatie bij het vrijen aanwezig was, na deze operatie geheel verdwenen. Bij 93% van de patiënten was de situatie ten aanzien van de prolaps een jaar na de operatie beter of heel veel beter dan voor de operatie.

Hoofdstuk 5 beschrijft de 1-jaar resultaten van 128 patiënten die voor een stadium III prolaps werden behandeld met een gedeeltelijk oplosbare polypropyleen mesh. Dit observationele onderzoek werd uitgevoerd in 11 centra verspreid over Europa en de Verenigde Staten. Het betrof ook hier ook een trocar-geleide spanningsvrije mesh behandeling, maar met een mesh die enigszins elastisch was, met name in lengte richting en bestond uit gelijke delen van onoplosbaar polypropyleen en oplosbaar polyglecaprone 25. Voor volledige resorptie is het mesh gewicht 57 gr/m^2 en na volledige absorptie na 90-120 dagen slechts 31 gr/m^2.

Anatomisch succespercentage na één jaar was 77.4% (69-84); niet significant verschillend van de tot die tijd gebruikte niet resorbeerbare polypropyleen mesh. De functionele uitkomsten waren eveneens goed en seksuele functie, gemeten met de PISQ-12 vragenlijst, was significant verbeterd een jaar na de ingreep.

Bij slechts 2% van de patiënten kon *de novo* pijn bij het vrijen worden gedocumenteerd. Negenentachtig procent van de patiënten ervoer haar prolaps situatie een jaar na de ingreep als beter of heel veel beter. De behandeling bleek veilig en er waren geen klinische aanwijzingen voor het bestaan van zogenaamde 'mat-krimp'.

Hoofdstuk 6 vergelijkt het seksueel functioneren, uitgedrukt in gemiddelde PISQ-12 scores, bij patiënten die wegens een recidief verzakking een spanningsvrije mesh behandeling ondergingen of een klassieke behandeling met lichaamseigen weefsel. Deze studie was een secundaire analyse van studie VROUW I, een gerandomiseerd onderzoek dat tot doel had anatomische uitkomsten te vergelijken van het behandelde vaginale compartiment bij patiënten met een recidief prolaps, die of een conventionele prolaps plastiek met lichaamseigen weefsel ondergingen of een trocar-geleide spanningsvrije mesh behandeling (de Prolift™ procedure). Van de 194 geincludeerde patiënten waren er 78 in de mesh arm en 50 in de lichaamseigen arm seksueel actief. Zestig patiënten hadden zowel voor als een jaar na de operatie de PISQ-12 vragenlijst geheel ingevuld, 58 slechts voor *of* na, maar niet beide. De laatste 58 werden geclassificeerd als uitvallers en vergeleken met de groep die wel volledig had gerespondeerd.

Wij konden na een jaar geen verschil in totale PISQ-12 score waarnemen tussen beide groepen. Wel observeerden wij een verschillend effect van de behandelingen op seksuele functie. De 'lichaamseigen' groep vertoonde een hogere postoperatieve totale PISQ score, die geheel kon worden verklaard door significante verbeteringen in de fysieke en partnergerelateerde subschalen. De totale PISQ-12 score bleef pre- en postoperatief gelijk in de mesh groep. Verbeteringen in de fysieke subschalen werden hier teniet gedaan door verslechteringen in de gedrag/emotie gerelateerde subschalen. Het waren vooral afnamen in de frequentie van orgasme en het opgewonden raken die hiervoor verantwoordelijk waren.

De verklaring voor deze bevinding wordt gezocht in het mogelijk negatieve effect dat de insertie een synthetische mesh heeft op de fysiologische respons op seksuele stimuli van de vagina. Verder werd geopperd als verklaring dat het lichaamsbeeld dat patiënten van zichzelf hebben in de mesh arm ten nadele was veranderd, of het lichaamsbeeld dat de mannelijke partner kreeg van zijn vrouw die met mesh werd behandeld.

Het bleek dat de aanwezigheid van een mesh '*exposure* voorspellend was voor verslechtering van de seksuele functie score, gemeten met de PISQ-12.

Hoofdstuk 7 handelt over de vergelijking van verschillende anatomische uitkomst definities voor falen in prolaps chirurgie. De traditioneel gebruikelijke *NIH Workshop* uitkomstmaten voor falen (POP stage ≥ II) werden vergeleken met een nieuwe, klinisch meer relevante, samengestelde uitkomstmaat voor falen (prolaps van enig vagina compartiment voorbij het hymen *met* de aanwezigheid van een

balgevoel of een re-interventie voor prolaps). In deze prospectieve cohort studie van 433 patiënten, die werden behandeld met trocar-geleide spanningsvrije mesh, varieerden de faal uitkomsten van 9% (7-13) voor de samengestelde uitkomst tot 41% (36-45) voor de conventionele NIH uitkomst voor prolaps in enig compartiment van de vagina. De samengestelde uitkomstmaat voor falen verschilde niet significant van de NIH uitkomst voor het met mesh behandelde vaginale compartiment (15%, 12-19). Aangezien de samengestelde uitkomstmaat de aanwezigheid van *balgevoel* bij patiënten meeneemt, bevelen wij het gebruik van deze uitkomstmaat sterk aan in toekomstig wetenschappelijk onderzoek.

Het tweede doel van de studie was het identificeren van voorspellers voor falen in deze verschillende uitkomstmaten met de hulp van logistische regressie analyse. Onafhankelijke voorspeller voor falen in alle uitkomstmaten bleek de gecombineerde anterior/posterior mesh behandeling met behoud van de baarmoeder te zijn.

Hoofdstuk 8 is een algemene discussie over de onderzoek bevindingen van dit proefschrift. Ook worden uitdagende nieuwe onderzoek mogelijkheden rondom genitale prolaps geopperd, die o.a. betrekking hebben op de etiologie, de preventie en de behandeling.

10

ADDENDUM

LIST OF ABBREVIATIONS IN ALPHABETICAL ORDER

CI	Confidence Interval
DDI	Defecatory Distress Inventory
DKL	Defaecatie Klachten Lijst
EQ5D	Euroquol-5D
FSFI	Female Sexual Function Index
IIQ	Incontinence Impact Questionnaire
IKL	Impact Klachten Lijst
NIH	National Institute of Health
PGI-I	Patients' Global Impression of Improvement
PISQ	Prolapse and Incontinence Sexual Function Questionnaire
PFDI	Pelvic Floor Distress Inventory
PFIQ	Pelvic Floor Impact Questionnaire
POP	Pelvic Organ Prolapse
POP-Q	Pelvic Organ Prolapse Quantification
TVM	Tension-free Vaginal Mesh
UDI	Urinary Distress Inventory
UKL	Plas Klachten Lijst

QUESTIONNAIRES

INSTRUCTIE

Geachte mevrouw,
Voor u ligt de vragenlijst die u hebt ontvangen van uw behandelende gynaecoloog. De vragenlijst is bedoeld om meer inzicht te krijgen in uw problematiek en om het effect van de voorgestelde behandeling te kunnen meten. In Nederland wordt het gebruik van deze vragenlijst aanbevolen door de Werkgroep Bekkenbodem van de Nederlandse Vereniging voor Obstetrie en Gynaecologie. De vragenlijst bestaat uit een aantal onderdelen. Deze onderdelen bevatten soms vragen waarvan u misschien denkt dat ze niet van belang zijn. Wij verzoeken u echter wel om **alle** vragen in te vullen tenzij anders vermeld. Het invullen duurt ongeveer 10 minuten

Naam:
Geboortedatum:
Lengte:
Gewicht:
Datum van invullen:

Dit deel van de vragenlijst bevat een aantal algemene vragen. Omcirkel het bij u passend antwoord of vul het getal in.

---

1. Wat is uw leeftijd? jaar

2. Welke opleiding(en) heeft u voltooid? (meer dan één antwoord mogelijk)
   1. basisonderwijs / lagere school (of een deel daarvan)
   2. lager beroepsonderwijs (lts, lhno, leao, huishoudschool etc.)
   3. mavo, (m)ulo etc.
   4. middelbaar beroepsonderwijs (mts, meao, opleiding tot verpleegkundige etc.)
   5. vwo, havo, gymnasium, mms etc.
   6. hoger beroepsonderwijs (hts, heao, sociale academie etc.)
   7. wetenschappelijk onderwijs (doctoraal examen)

3. Wat is uw huidige beroep of zijn uw werkzaamheden?

4. a. Hebt u kinderen?

1. Ja	0 Nee (ga door met vraag 5)	
b. Hoeveel kinderen heeft u?		(aantal)
c. Hebt u een keizersnede gehad?	1 Ja (keer)	0 Nee
d. Hebt u een tang verlossing gehad?	1 Ja (keer)	0 Nee
e. Hebt u een vacuüm cup verlossing gehad?	1 Ja (keer)	0 Nee
f. Bent u tijdens de bevalling "ingeknipt"	1 Ja (keer)	0 Nee
g. Bent u tijdens de bevalling "ingescheurd"	1 Ja (keer)	0 Nee
h. Wanneer was uw laatste bevalling?		(dag/maand/jaar)
e. Hoe oud was u tijdens de eerste bevalling		(leeftijd in jaren)

Bij de volgende vraag loopt de antwoordcategorieën op van 1 (erg slecht) tot 6 (uitstekend).
Wilt u het getal omcirkelen dat het meest op u van toepassing is?

---

5. Hoe zou u uw algehele kwaliteit van leven gedurende de afgelopen week beoordelen?

1	2	3	4	5	6
Erg slecht					uitstekend

De volgende 5 vragen hebben betrekking op uw huidige gezondheidstoestand. Omcirkel bij elke vraag de zin die het best past bij uw eigen gezondheidstoestand vandaag.

6a. Mobiliteit

1. Ik heb geen problemen met lopen
2. Ik heb enige problemen met lopen
3. Ik ben bedlegerig

6b. Zelfzorg

1. Ik heb geen problemen om mijzelf te wassen of aan te kleden
2. Ik heb enige problemen om mijzelf te wassen of aan te kleden
3. Ik ben niet in staat mijzelf te wassen of aan te kleden

6c. Dagelijkse activiteiten(bv werk, studie, huishouden, gezin- en vrijetijdsactiviteiten)

1. Ik heb geen problemen met mijn dagelijkse activiteiten
2. Ik heb enige problemen met mijn dagelijkse activiteiten
3. Ik ben niet in staat mijn dagelijkse activiteiten uit te voeren

6d. Pijn/klachten

1. Ik heb geen pijn of andere klachten
2. Ik heb matige pijn of andere klachten
3. Ik heb zeer ernstige pijn of andere klachten

6e. Stemming

1. Ik ben niet angstig of somber
2. Ik ben matig angstig of somber
3. Ik ben erg angstig of somber

6f.
Om mensen te helpen bij het aangeven hoe goed of hoe slecht een gezondheidstoestand is, hebben we een meetschaal (te vergelijken met een thermometer) gemaakt. Op de meetschaal hiernaast betekent "100" de beste gezondheidstoestand die u zich kunt voorstellen, en "0" de slechtste gezondheidstoestand die u zich kunt voorstellen.

We willen u vragen op deze meetschaal aan te geven hoe goed of hoe slecht volgens u uw eigen gezondheidstoestand vandaag is. Trek een lijn van het hokje hieronder naar het punt op de meetschaal dat volgens u aangeeft hoe goed of hoe slecht uw gezondheidstoestand vandaag is.

Uw gezondheidstoestand vandaag

Vrouwen met ongewenst urineverlies en / of een verzakking hebben aangegeven dat ze de volgende klachten hadden. Kunt u aangeven welke klachten u op dit moment ook heeft en hoeveel last u daar van heeft. Beantwoord svp alle vragen, ook als u geen klachten heeft.

---

7. a. Vindt u dat u vaak moet plassen?
    1. Ja
    2. Nee (ga naar 7c.)

   b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

   c. Hoe veel keer plast u gemiddeld per dag?: keer

8. a. Als u moet plassen voelt u dan altijd een sterke aandrang?
    1. Ja
    2. Nee (ga naar 9.)

   b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

9. a. Hebt u ongewenst urineverlies als u aandrang voelt om te plassen?
    1. Ja
    2. Nee (ga naar 10.)

   b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

   c. Zo ja, hoe vaak verliest u ongewild urine?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

10. a. Hebt u ongewenst urineverlies bij lichamelijke inspanning, hoesten of niezen?
    1. Ja
    2. Nee (ga naar 11.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

    c. Zo ja, hoe vaak verliest u ongewild urine?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

11. a. Hebt u moeite uw blaas leeg te plassen?
    1. Ja
    2. Nee (ga naar 12.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

12. a. Hebt u wel eens het gevoel dat de blaas na het plassen niet helemaal leeg is?
    1. Ja
    2. Nee (ga naar 13.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

13. a. Hebt u wel eens een drukkend gevoel onder in de buik?
    1. Ja
    2. Nee (ga naar 14.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

14. a. Hebt u wel eens pijn onder in de buik of in de schaamstreek?
    1. Ja
    2. Nee (ga naar 15.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

15. a. Hebt u wel eens het gevoel dat er iets uit de vagina stulpt?
    1. Ja
    2. Nee (ga naar 16.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

16. a. Hebt u wel eens gezien dat er iets uit de vagina stulpt?
    1. Ja
    2. Nee (ga naar 17.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

17. Hoe vaak hebt u het afgelopen jaar een blaasontsteking gehad?
    1. Nooit
    2. 1 keer
    3. tussen de 2 en 4 keer
    4. meer dan 4 keer

18. a. Moet u ‘s nachts meer dan 1 keer plassen?
    1. Ja
    2. Nee (ga naar 19.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

De navolgende verschijnselen zijn beschreven door vrouwen met klachten van de stoelgang. Geeft u aan welke verschijnselen u tegenwoordig herkent en hoeveel last u daarvan heeft.

---

19. a. Hebt u minder dan driemaal per week ontlasting?
    1. Ja
    2. Nee (ga naar 20.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

20. a. Moet u om ontlasting te krijgen in meer dan een kwart van de keren persen?
    1. Ja
    2. Nee (ga naar 21.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

21. a. Hebt u wel eens aandrang tot ontlasting terwijl er dan op het toilet geen ontlasting komt?
    1. Ja
    2. Nee (ga naar 22.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

22. a. Hebt u wel eens het gevoel dat er iets uit de anus hangt of er iets voor zit?
    1. Ja
    2. Nee (ga naar 23.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

23. a. Ervaart u pijn tijdens de aandrang tot ontlasting?
    1. Ja
    2. Nee (ga naar 24.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

24. a. Ervaart u pijn tijdens of vlak na de ontlasting?
    1. Ja
    2. Nee (ga naar 25.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

25. a. Verliest u wel eens dunne ontlasting zonder dat u daar controle over heeft?
    1. Ja
    2. Nee (ga naar 26.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

    c. Hoe vaak komt het voor?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

26. a. Verliest u wel eens vaste ontlasting zonder dat u daar controle over heeft?
    1. Ja
    2. Nee (ga naar 27.)

    b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

c. Hoe vaak komt het voor?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

27. a. Verliest u wel eens windjes zonder dat u daar controle over heeft?
    1. Ja
    2. Nee (ga naar 28.)

b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

c. Hoe vaak komt het voor?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

28. a. Moet u wel eens via de schede mee drukken om ontlasting te krijgen?
    1. Ja
    2. Nee (ga naar 29.)

b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

29. a. Moet u de ontlasting wel eens met de vingers via de anus verwijderen?
    1. Ja
    2. Nee (ga naar 30.)

b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

Sommige vrouwen vinden dat ongewenst urineverlies en/of een verzakking en/of problemen met de ontlasting hun activiteiten, relaties en gevoelens kunnen beïnvloeden. De vragen in onderstaande lijst gaan over aspecten van uw leven die door uw probleem beïnvloed of veranderd kunnen zijn. Geef voor iedere vraag het antwoord aan dat het beste beschrijft hoe zeer uw activiteiten, relaties en gevoelens beïnvloed worden door uw urineverlies en/of verzakking en/of problemen met de ontlasting.

Hoeveel invloed heeft ongewenst urineverlies en/of verzakking en/of problemen met de ontlasting gehad op:

30. Uw vermogen om huishoudelijk werk te doen (koken, schoonmaken, wassen)
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

31. Uw vermogen om klein onderhoud of reparaties te verrichten in en om het huis
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

32. Boodschappen doen en winkelen
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

33. Reizen met auto of openbaar vervoer over een afstand van minder dan 20 minuten
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

34. Ergens naar toe gaan als u niet helemaal zeker weet of er daar toiletten zijn
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

35. Bezoek krijgen van vrienden en kennissen
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

36. Relaties met vrienden en kennissen
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

37. Vermogen om een seksuele relatie te hebben
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

38. Geestelijke / emotionele gezondheid
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

39.Wordt u in uw activiteiten beperkt door angst dat anderen u ruiken?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

Hebt u als gevolg van uw probleem de volgende gevoelens?

40. Nervositeit of ongerustheid
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

41. Frustratie
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

42. Zich gegeneerd voelen
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

De volgende vragen gaan over de seksualiteit. Het is de bedoeling dat u bij het beantwoorden denkt aan de situatie van de afgelopen maand. Wilt U het voor u meest passende antwoord omcirkelen.

---

43. a. Hebt u wel eens seksueel contact met uw partner? (Denk hierbij aan *alle vormen* van seksueel contact en niet alleen aan geslachtsgemeenschap)
        1. Ja (beantwoord ook vraag b)
        2. Nee (beantwoord ook vraag 43c)
    b. Zo ja, hoe tevreden bent u daarover?
        1. Helemaal niet
        2. Een beetje
        3. Nogal
        4. Heel erg
    c. Zo nee, hoe vervelend vindt u dat?
        1. Helemaal niet
        2. Een beetje
        3. Nogal
        4. Heel erg

44. Hoe vaak hebt u geslachtsgemeenschap?
    1. Nooit
    2. minder dan 1 keer per maand
    3. 1 tot 2 keer per maand
    4. 1 keer per week
    5. meerdere keren per week

45. a. Verliest u wel eens urine tijdens de geslachtsgemeenschap?
        1. Ja
        2. Nee (ga naar 46.) 99 Niet van toepassing (geen seks)
    b. Zo ja, hoeveel last heeft u hier van?
        1. Helemaal niet
        2. Een beetje
        3. Nogal
        4. Heel erg

46. a. Ervaart u pijn tijdens de geslachtsgemeenschap?
    1. Ja
    2. Nee (ga naar 47.) 99 niet van toepassing (geen seks)

b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

47. a. Is de vagina zo nauw dat geslachtsgemeenschap daardoor niet mogelijk is?
    1. Ja
    2. Nee 99 niet van toepassing (geen seks)

b. Zo ja, hoeveel last heeft u hier van?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

Heeft u **alle vragen** ingevuld?
Hartelijk dank!

Vragenlijst seksueel functioneren bij verzakking en ongewenst urineverlies (korte versie: PISQ-12)

Vraag vooraf: Bent u seksueel actief?

Ja; ga verder met het lezen van de instructie en invullen van de vragenlijst
Nee; deze vragenlijst is niet voor u van toepassing

Instructie. Voor u ligt een lijst met vragen over het seksueel leven van u en uw partner. Alle informatie is strikt vertrouwelijk. Uw vertrouwelijke antwoorden zullen alleen worden gebruikt om artsen inzicht te geven in wat belangrijk is voor patiënten in hun seksueel leven. Kruist u alstublieft aan wat voor u het beste antwoord is op de vraag. Bij het beantwoorden van de vragen gaat u uit van uw seksueel leven van de afgelopen 6 maanden. Bedankt voor het invullen.

1. Hoe vaak verlangt u naar seks? Dit verlangen kan bestaan uit het willen hebben van seks, het plannen van seks, gevoelens van frustratie door een gebrek aan seks, enzovoorts.
   Dagelijks
   Wekelijks
   Maandelijks
   Minder dan 1 keer per maand
   Nooit

2. Heeft u een orgasme tijdens geslachtsgemeenschap met uw partner?
   Altijd
   Meestal
   Soms
   Zelden
   Nooit

3. Voelt u zich seksueel opgewonden tijdens seksuele activiteiten met uw partner?
   Altijd
   Meestal
   Soms
   Zelden
   Nooit

4. Hoe tevreden bent u over de afwisseling in seksuele activiteiten in uw huidige seksleven?

Zeer tevreden
Redelijk tevreden
Noch tevreden, noch ontevreden
Redelijk ontevreden
Zeer ontevreden

5. Heeft u pijn tijdens geslachtsgemeenschap?

Altijd
Meestal
Soms
Zelden
Nooit

6. Heeft u ongewenst urineverlies tijdens seksuele activiteiten?

Altijd
Meestal
Soms
Zelden
Nooit

7. Wordt u in uw seksuele activiteiten beperkt door angst voor ongewenst verlies van ontlasting of urine?

Altijd
Meestal
Soms
Zelden
Nooit

8. Vermijdt u geslachtsgemeenschap vanwege een uitstulping in de vagina (verzakking van blaas, endeldarm of vagina)?

Altijd
Meestal
Soms
Zelden
Nooit

9. Wanneer u seks heeft met uw partner, heeft u dan negatieve emotionele reacties, zoals angst, afkeer, schaamte of schuldgevoel?

Altijd
Meestal
Soms
Zelden
Nooit

10. Heeft uw partner een erectieprobleem dat uw seksuele activiteiten beïnvloedt?

Altijd
Meestal
Soms
Zelden
Nooit

11. Heeft uw partner een probleem met voortijdige zaadlozing dat uw seksuele activiteiten beïnvloedt?

Altijd
Meestal
Soms
Zelden
Nooit

12. Hoe intens zijn de orgasmen die u in de afgelopen 6 maanden heeft gehad in vergelijking met orgasmen in het verleden?

Veel minder intens
Minder intens
Dezelfde intensiteit
Meer intens
Veel meer intens

13. a. Bent u tevreden met uw seksueel functioneren?

Ja, ik ben tevreden
Neen; ga door met beantwoording van vraag 13b

b. Levert dit stress op voor u en/of stress in uw relatie? (alleen invullen als u 13. a met neen hebt beantwoord)

Altijd
Meestal
Soms
Zelden
Nooit

INSTRUCTIE

Geachte mevrouw,
Deze vragenlijst is bedoeld om de situatie **na** de behandeling die u hebt ondergaan te vergelijken met de situatie zoals die **vóór** de behandeling bestond. Daarom begint deze vragenlijst met een algemene vraag naar de **mate van verbetering** die de behandeling bij u heeft teweeg gebracht. De overige vragen zijn identiek aan die uit de eerste vragenlijst, waarbij de eerste vier daar gestelde vragen om begrijpelijke redenen niet behoeven te worden herhaald. Daarom gaat deze vragenlijst hierna voort met **vraag 5**. Wij verzoeken u dus om na beantwoording van de eerste vraag door te gaan met **vraag** nummer **5** en ook dit keer weer **alle** volgende vragen in te vullen.

Naam:
Geboortedatum:
Lengte:
Gewicht:
Datum van invullen:

Deze vraag geeft een globale indruk over de mate van verbetering die de behandeling bij u heeft teweeg gebracht. Omcirkel het getal dat het meest op uw huidige situatie van toepassing is.

U heeft een behandeling ondergaan voor uw plas- en/of verzakkingsklachten.
Kies uit het onderstaande rijtje het antwoord dat het beste weergeeft hoe uw situatie **nu** is ten opzichte van de situatie zoals die was vóórdat u werd behandeld.

1. heel veel beter
2. veel beter
3. beetje beter
4. geen verandering
5. beetje slechter
6. veel slechter
7. heel veel slechter

Hierna is de vragenlijst identiek aan de intake vragenlijst vanaf vraag 5

PFDI-20

Vrouwen met ongewenst urineverlies en/of een verzakking hebben aangegeven dat zij de volgende klachten hadden. Kunt u aangeven welke klachten u op dit moment ook heeft en hoeveel last u daarvan heeft. Beantwoord svp alle vragen, ook als u geen klachten heeft.

---

1. a. Voelt u vaak een *drukkend gevoel* in uw onderbuik?
    1. Ja
    2. Nee

   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

2. a. Heeft u vaak een *zwaar* of *dof gevoel* in uw bekken?
    1. Ja
    2. Nee

   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

3. a. Voelt of ziet u vaak dat er iets uit het gebied rond de vagina stulpt of valt?
    1. Ja
    2. Nee

   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

4. a. Moet u vaak op de vagina of rond het rectum drukken om uw ontlasting eruit te helpen?
    1. Ja
    2. Nee

b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

5. a. Heeft u vaak het gevoel dat uw blaas na het plassen niet helemaal leeg is?
    1. Ja
    2. Nee
   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

6. a. Moet u wel eens met uw vingers op een uitstulping in het gebied rond de vagina drukken om ervoor te zorgen dat u kunt beginnen met plassen of uit kunt plassen?
    1. Ja
    2. Nee
   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

De navolgende verschijnselen zijn beschreven door vrouwen met klachten van de stoelgang.
Geeft u aan welke verschijnselen u tegenwoordig herkent en hoeveel last u daarvan heeft.

---

7. a. Heeft u wel eens het gevoel dat u te hard moet persen om uw ontlasting kwijt te raken?
    1. Ja
    2. Nee
   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

8. a. Heeft u wel eens het gevoel dat uw darmen na de stoelgang niet helemaal leeg zijn?
    1. Ja
    2. Nee

   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

9. a. Verliest u wel eens vaste ontlasting zonder dat u daar controle over hebt?
    1. Ja
    2. Nee

   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

   c. Hoe vaak komt dit voor?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

10. a. Verliest u wel eens dunne of vloeibare ontlasting zonder dat u daar controle over hebt?
    1. Ja
    2. Nee

   b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

   c. Hoe vaak komt dit voor?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

11. a. Laat u wel eens windjes zonder dat u daar controle over hebt?
    1. Ja
    2. Nee

    b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

    c. Hoe vaak komt dit voor?
    1. dagelijks
    2. paar keer per week
    3. 1 keer per week
    4. 1 keer per maand
    5. 1 keer per jaar

12. a. Heeft u tijdens de stoelgang pijn?
    1. Ja
    2. Nee

    b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

13. a. Voelt u vlak voor de stoelgang sterke aandrang en moet u dan zo snel mogelijk een wc opzoeken?
    1. Ja
    2. Nee

    b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

14. a. Komt het tijdens of vlak na de stoelgang wel eens voor dat een stukje darm uit het rectum naar buiten stulpt?
    1. Ja
    2. Nee

    b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

15 a. Moet u vaak plassen?
1. Ja
2. Nee (ga naar 15c.)

b. Zo ja, hoeveel last hebt u hiervan?
1. Helemaal niet
2. Een beetje
3. Nogal
4. Heel erg

c. Hoeveel keer plast u gemiddeld per dag?: keer

16. a. Heeft u ongewenst urineverlies als u aandrang voelt om te plassen?
1. Ja
2. Nee

b. Zo ja, hoeveel last heeft u hiervan?
1. Helemaal niet
2. Een beetje
3. Nogal
4. Heel erg

c. Zo ja, hoe vaak verliest u ongewild urine?
1. dagelijks
2. een paar keer per week
3. één keer per week
4. één keer per maand
5. één keer per jaar.

17. a. Verliest u urine als u moet hoesten, niezen of lachen?
1. Ja
2. Nee

b. Zo ja, hoeveel last heeft u hiervan?
1. Helemaal niet
2. Een beetje
3. Nogal
4. Heel erg

c. Zo ja, hoe vaak verliest u ongewild urine?
1. dagelijks
2. een paar keer per week
3. één keer per week
4. één keer per maand
5. één keer per jaar.

18. Verliest u vaak kleine hoeveelheden urine, dat wil zeggen druppeltjes?
1. Ja
2. Nee

b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

19. Heeft u vaak moeite om uw blaas te legen?
    1. Ja
    2. Nee

b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

20. Ervaart u vaak pijn of ongemak in de onderbuik of de schaamstreek?
    1. Ja
    2. Nee

b. Zo ja, hoeveel last heeft u hiervan?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

PFIQ-7

Sommige vrouwen vinden dat ongewenst urineverlies en/of een verzakking en/of problemen met de ontlasting hun activiteiten, relaties en gevoelens kunnen beïnvloeden. De vragen in onderstaande lijst gaan over aspecten van uw leven die door uw probleem beïnvloed of veranderd kunnen zijn. Geef voor elke vraag het antwoord aan dat het beste beschrijft hoe zeer uw activiteiten, relaties en gevoelens beïnvloed worden door uw urineverlies en/of verzakking en/of problemen met de ontlasting.

Hoeveel invloed heeft ongewenst urineverlies en/of verzakking en/of problemen met de ontlasting gehad op:

1. Uw vermogen om huishoudelijk werk te doen (koken, schoonmaken, wassen)?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

2. Uw vermogen lichamelijke activiteiten te ondernemen zoals wandelen, zwemmen of andere oefeningen?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

3. Het bezoeken van een uitvoering zoals een film of een concert?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

4. Uw vermogen met de auto of de bus te reizen, langer dan 30 minuten van huis?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

5. Uw deelname aan sociale activiteiten buitenshuis?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

6. Uw emotionele gezondheid (nervositeit, depressie enz.)?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

7. Gevoelens van frustratie?
    1. Helemaal niet
    2. Een beetje
    3. Nogal
    4. Heel erg

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ABOUT THE AUTHOR

Alfredo Lorenzo Milani was born on May 11th 1955 in Dordrecht, the Netherlands, as the eldest son of Geziena Maria Zalm (*04.02.1929, †29.06.2011) and Nicodemo Lorenzo Milani (*12.01.1929). In 1972 he graduated from high school (HBS-B: Titus Brandsma College) in Dordrecht. Unfortunately he was eliminated 'by lottery' for Medical School in the Netherlands, but could start this study at the University of Antwerp (RUCA) in Belgium. After completing the propaedeutic course cum laude, he was offered a restart of study in the Netherlands at the Erasmus University Medical School Rotterdam. During this study he was a student-assistant in Physics and Neuro--Anatomy. The latter created the opportunity to follow a junior residency Neurology at the Albert Einstein College of Medicine, New York in 1976.

After graduation from Medical School in 1979, he prepared himself for Tropical Medicine. After finishing the necessary residencies in Obstetrics & Gynecology (Ikazia Hospital Rotterdam) and Surgery (Hofpoort Hospital Woerden), as well as a Postgraduate Course in Tropical Medicine and Kiswahili language course at the Royal Institute for the Tropics in Amsterdam, he left for Tanzania in 1982. There he worked at the Rubya Designated District Hospital in Northwest Tanzania for 4 years. His eldest daughter and son were born on African soil.

Having become motivated for Obstetrics & Gynecology in Africa, he started his Training residency at the Ikazia Hospital Rotterdam -where his youngest son was born- and the Erasmus University Medical Center. At the Ikazia Hospital Mark Vierhout started sowing the seeds for his later interest in Urogynecology. After obtaining his registration as consultant in Obstetrics & Gynecology in 1993 he started working as general gynecologist at the Reinier de Graaf Hospital Delft, where he still is working today.

In 1998 he was invited by Mark Vierhout to participate in the organization of the National Urogynecology Course for last year residents in Obstetrics & Gynecology. He has been a board member since. In 2002 Mark Vierhout initiated a differentiation--year Urogynecology for last year residents and started the cooperation between the Erasmus University Medical Center and the Reinier de Graaf Hospital Delft. One of the residents that followed this differentiation-year was Mariella Withagen. In 2005 Mark Vierhout became the first professor in Pelvic Floor Pathology at the Radboud University and invited Mariella Withagen to become his staff member. That created the foundation for consistent and sound scientific cooperation between Nijmegen and Delft. This scientific cooperation *and* friendship forms the base of the work presented in this thesis.

Since 2010 he is president of the board of the Pelvic Floor Society of the Dutch Gynecologists and since 2011 registered as subspecialist in Urogynecology.

He is the blessed father of three children: Sara Zawadi (*01.11.1983), David Byera (*09.10.1985) and Nathan Lorenzo (*20.05.1992) and the partner of Bart Broekman.

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